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# Informed Consent for Research in Life-limiting Diseases: Overcoming Therapeutic Misconception

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**Abstract**

Informed consent is central to ethical research, but ensuring it is both truly 'informed' and 'voluntary' is challenging. Life-limiting, progressive diseases affecting children pose particular difficulties, particularly in avoiding the risk of therapeutic misconception. Digital technologies may help to reduce misconception between researchers, participants, and their families. By monitoring interaction with such technologies, participant and family comprehension of the research protocol may be ascertained, and potential therapeutic misconception flagged to the researcher for further discussion. Although this may reduce initial recruitment in a research project, we suggest that retention may be improved, as participants will be better informed. Furthermore, such an approach is in line with the underlying intent of informed consent.

**Author Keywords**

Informed consent; therapeutic misconception; ethics; research, Duchenne muscular dystrophy; rare diseases; trials

**Introduction**

Ensuring informed consent in medical research is truly 'informed' and 'voluntary' is challenging, particularly in

relation to progressive, life-limiting disorders affecting children. We examine the issues surrounding clinical trials for a vulnerable participant group, and – given the existing role played by technology in information provision and community relations for this group – consider the ways in which technology might be used to help to reconfigure the consent process.

### **Informed Consent in Medical Research**

Informed consent is essential to ethical and legitimate medical research. It is embedded in professional codes of conduct for clinicians and in the ethical approval process for medical research [3, 10-12, 19]. Informed consent aims to protect an individual's freedom of choice on whether or not to take part in research, and to respect that person's autonomy. Particularly important is that the individual is capable to consent, has received and understood necessary information, and has arrived a decision on whether to or not to participate without coercion, undue influence or inducement, or intimidation [3].

Despite its centrality to modern clinical research practice, there are recognised issues around informed consent. Previous work has found that participants often misunderstand aspects of the research endeavor in both the developing and developed world [18]. In particular, it is sometimes difficult to ascertain whether a participant in research is truly 'informed', and whether their participation is indeed 'voluntary' [6]. The former may be compromised by highly complex medical knowledge needed to understand the potential treatment under investigation, and the accompanying research protocols, both of which require communication to the participant in a way that they understand. In certain situations, such as life-limiting,

progressive conditions with no effective treatment, participant 'choice' may be influenced by diverse factors. Deciding to take part may be less voluntary than it would at first seem, particularly if there is an unclear understanding of the research process on the part of the participant.

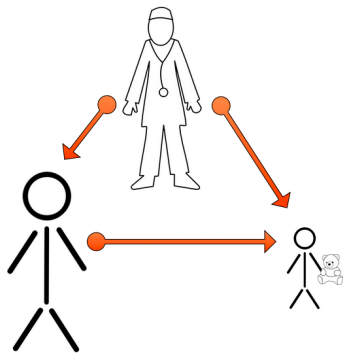
Ensuring research participants have a clear understanding of the nature of their participation is challenging. Of particular concern is what Appelbaum *et al* [1] identified as "therapeutic misconception", where patients failed to appreciate the difference between research and treatment. This is described by Henderson *et al* [15] as occurring "when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial". The false belief that the central purpose of the trial is therapeutic, and that the individual will personally benefit, may even be held to undermine and thus disqualify the 'informed' nature of their consent [24].

Various studies have been undertaken to study the factors influencing prospective research participants' levels of understanding, but a systematic review of these has found that improved understanding via multimedia and enhanced consent forms have met with only limited success [9].

### **Vulnerable Groups**

Healthy children and young people are considered a vulnerable group, necessitating particular caution in a research context [22], with additional safeguards required in medical [10] and clinical research [6, 13].

Although parents are obliged to provide consent, best practice is to gain agreement ('assent') from the child. However, this approach is not without controversy and some have even argued that it is "ill thought-out, confused and harmful", calling instead for children with 'competence' to provide true consent, with consent for those considered 'incompetent' being provided solely by their parents [20].



**Figure 1:** A stylized illustration of the existing decision-making process between clinician, parent, and child participant. Note the unequal power relationship between the clinician (top) and family, and between parent and child.

This issue highlights the power relationships that are involved when children participate in medical research: between the parent and the child, the researcher and the parent, and the researcher and the child (*Figure 1*). In engaging with the role of power in the research process, participatory research approaches are acknowledged as challenging to conduct amongst children with chronic health issues [5]. Furthermore, children with life-limiting rare diseases pose specific challenges in research. In clinical trials there may be a combination of the aforementioned therapeutic misconception, parental grief, and the blurring of the boundaries between research and treatment, as there is often an overlap in personnel between research and clinical teams. These factors have been suggested as contributing towards the high enrolment of children in early-stage paediatric oncology trials [13].

In these circumstances there is clearly significant potential for therapeutic misconception, often amongst parents [24]. We consider one disease, Duchenne muscular dystrophy (DMD), as embodying particular concerns in this regard.

#### *Duchenne Muscular Dystrophy*

DMD is an inherited, life-limiting muscle-wasting disease affecting as many as 1 in 3,600 boys [2].

Children with DMD have difficulty standing up, climbing, and running, lose the ability to walk by their teenage years, and experience increasing lung and heart complications over time. Life-expectancy has significantly improved with better care, with many individuals living into their thirties or even forties. However, there is still no curative treatment and DMD remains a serious condition requiring round-the-clock care assistance and frequent medical checkups in adulthood.

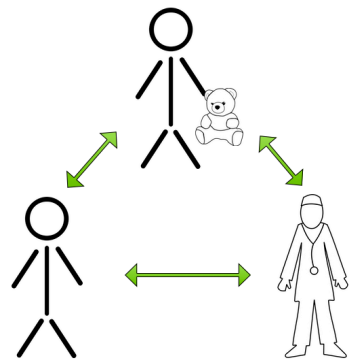
A highly active international DMD patient community has developed that raises public awareness, campaigns on behalf of and funds research into the disease, and provides support and information to those living with the condition and their families [21]. A particular concern is halting the debilitating and inexorable decline of those living with the condition. As with many rare diseases, patients and their families have become knowledgeable and credible activists [25], well informed about the disease and the wide range of cutting edge treatment strategies that currently under development. Yet even in this well-informed community, therapeutic misconception remains a possibility [24]. For other more common diseases with a less actively engaged patient and family population, this is even more the case.

#### *Online Communities for DMD*

Online patient communities permit the exchange of a range of different forms of support [4]. Such technology already plays an important role to many rare disease groups, enabling networking and information sharing amongst a geographically disparate community [7]. DMD organisations are no exception: they co-ordinate web forums and run webinars (often in

conjunction with researchers), to disseminate the latest knowledge to the community. As such, technology assists in a process of apomediation where community members access and share knowledge between their peers rather than solely through traditional gatekeepers such as clinicians [8]. Patient peer expertise has distinct characteristics that differ from and complement the expertise of health professionals [14], and such perspectives may be very valuable in the context of clinical trials for rare diseases.

There have already been attempts by the broader neuromuscular community, of which the DMD community is an important part, to highlight ethical issues in relation to clinical trials and emerging potential therapies and publicise these to as broad an audience as possible via the Internet [23]. It is clear, therefore, that technology has an important role to play in facilitating the transfer of knowledge in rare diseases. Yet as one recent review has noted, there has been limited use of technology “to engage with research participants to facilitate participation in research on their terms or to encourage an interactive dialogue between research participants and researchers”, particularly around the question of consent [17]. This mirrors the separation previously identified in online health communities between peer and clinical expertise [16]. There is therefore an opportunity to use technology to develop a more participatory or democratic process of consent that may tackle the aforementioned challenges associated with the context of progressive, life-limiting conditions such as DMD. Furthermore, encouraging participatory decision-making also has applicability with respect to treatment decisions and other aspects of the healthcare ‘journey’.



**Figure 2:** An ideal model of a decision-making process between child participant (top), parent, and clinician. Note that the child plays an equal role alongside their parent and the clinician.

## Future Directions

For technologies to support participatory consent processes and reduce possible therapeutic misconception, they must demonstrate the potential to improve both comprehension and understanding for potential participants over current models of informed consent. In this final section, we pose a series of opportunities and challenges for technology in this space.

### *Open questions and opportunities*

First, we ask whether it might be possible for technologies to help facilitate discussion between potential research participants, and between them and researchers (*Figure 2*). Social media, collaborative blogs, or other forms of online participatory media may provide the space for research participants to ask questions they feel uncomfortable posing in the context of a one-to-one interaction with a researcher or clinician with its attendant power imbalances. Of course, in many respects discussions such as these are already taking place online, in an unstructured and sometimes unmoderated manner. While these informal online discussions, which often take place with peers, have the potential to demystify and clarify aspects of participation in research, there is equally the potential for misinformation to be perpetuated. It is therefore worth investigating how technology might enable research teams to be involved in this process, and what it might mean to have open online dialogues between communities of research participants and those managing and facilitating the running of trials.

Second, we consider how technologies might play a role in facilitating children’s and families’ understanding of research. It is already acknowledged [10-12] that

clinicians and researchers should provide appropriately tailored information to participants and their families. It is also worth considering that only by being truly informed themselves can parents hope to provide appropriate information to their children. Specific technological interventions – such as age-appropriate interactive storybooks with multimedia content or even simple interactive games – might be used as part of an informed consent process to help to convey information to potential participants. Such technology might also warn the clinician, based on responses or actions, whether a particular participant’s understanding of the research to which they are consenting is unclear, and when issues such as therapeutic misconception might be present. These could then be flagged for further discussion by the researcher. We envisage such technologies as adjuncts to existing conversations, rather than replacements for the discussions that take place between potential participants and researchers.

Third, we speculate that the bringing together of new forms of dialogue between participants and researchers, and new tools for engaging people in understanding the nuances of trials in which they participate, opens up new models for configuring informed consent. We could imagine ways that at the start of a trial, participants are provided private but shared online spaces where they anonymously discuss their understandings of the planned trial with other potential participants. A trial might not commence until all potential consentees have engaged in discussion, or perhaps even only when all community members have demonstrated comprehension. Or, alternatively, participants might vote on when a trial should start based on an understanding at the community-level of what risks are associated with taking part. Community

members and early participants could perhaps help to contribute to revised consent information or processes based on their own understanding and participation.

### *Challenges*

There are many challenges to increasing the use of technologies within the consent process in an effort to make it more democratic. One is the possibility that through making such online discussion and dialogue mandatory to trial participation, we unnecessarily prevent potential participants from taking part. This is more than an issue of access to the necessary technologies: it may be that participants (or their parents), particularly in a progressive rare disease, would rather prioritize taking part in the trial as quickly as possible over a prolonged process of discussion and debate where they must ‘prove’ their understanding of the purpose of the research.

A further significant challenge to any such technology will be acceptance by regulatory bodies and research ethics committees. Clinical research on children in particular is tightly regulated, and all procedures (including details such as the wording of consent letters) must be approved for individual research projects. Ethics and regulatory approval would be needed if information were being changed in response to the understanding of early participants. The use of novel technologies in the manner and for the purposes we suggest might prove challenging for such bodies, at least until they are validated and widespread enough to become part of regular practice. However, we contend that as patients are gaining increasing insight about their condition and potential therapies or trials informally online, ethics committees should respond to

these wider societal changes and provide more adaptable and flexible consent processes.

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