Know Your Audience: Clinical Trials with Paediatric Populations

Planning for Paediatric Populations

In recent years the FDA has placed greater emphasis on the need for paediatric studies. A recent ClinicalTrials.gov search resulted in over 4000 studies actively recruiting paediatric populations in the US alone[1]. Clinical trials involving infants, children and/or adolescents require special consideration due to the developmental transitions that occur throughout this age range. Not only are children going through a number of physical changes, but they are also experiencing a host of emotional, social, and cognitive changes that can significantly impact the success of a trial. Of particular concern when conducting a clinical trial with children is health literacy; a patient's ability to comprehend and evaluate trial-related information in order to make informed decisions. Children are not 'little adults', and as paediatric studies continue to increase, the need for targeted, yet flexible, health literacy strategies is becoming evident.

Talking to young children of varying ages and social backgrounds about clinical trials can often be more difficult than talking to adults. While the age range in paediatric trials is usually no larger than that of adult trials, the developmental gap between a 5-year-old and a 15-year-old is large compared to a 50-year-old and a 60-year-old. Therefore, while a single strategy may be sufficient for adults (e.g., informational pamphlet or booklet); multiple, age-appropriate strategies are often necessary for children and adolescents. An additional level of complexity stems from the fact that paediatric health literacy cannot be considered in isolation from parents' and/or caregivers' health literacy. For instance, higher literacy skills in parents have been associated with better outcomes in child health promotion and disease prevention[2]. This may be due in part to the fact that adults with low health literacy have less interest in being involved in health-related conversations, ask fewer questions of healthcare professionals, and experience more uncertainty when making decisions[3]. Moreover, adults with low health literacy have been found to have lower rates of medication adherence[4]. In planning for paediatric trials, sites need to plan accordingly; having in place appropriate strategies able to meet the diverse needs of children, adolescents, and parents/caregivers.

Capacity for the Paediatric Audience to Process Information

While developmental change is thought to be a continuous process occurring gradually over time, for the purposes of planning and implementing a clinical trial, it can be helpful to categorise paediatric patients into three broad age groups:

- Young children aged 3-7 years
- Pre-teens aged 8-12 years
- Adolescents aged 13-17 years

The informational requirements of these three groups can be very different. While there can be common threads, it is important to recognise and understand the key drivers for each group.

Young children often do not have the cognitive resources to understand their disease or condition, nor its long-term implications. While it is vital that they are not made to feel afraid, there is no reason to exclude them from key discussions throughout the trial. This includes explaining in basic language why the family is making multiple visits to the hospital or clinic. Explanations around their condition should be kept as simple as possible and not become a roadblock to the child attending trial visits or receiving medical treatments.

As children get older, the amount of information they are able to understand increases. However, pre-teens may still find it difficult to comprehend what is happening, including why someone should take medications when they are not feeling sick. Being able to explain what is happening to them in language they understand is critical. Doctors and study nurses should describe what the trial will involve, such as trips to the hospital, getting blood samples taken, and any related treatments, such as injections. During the informed consent process their medical condition should be explained to them in age-appropriate terms and the importance of preventive treatment should be introduced.

Adolescents should be actively involved in their healthcare as much as possible. It is important that this age group feels a sense of ownership and control over what is happening to them. Depending on their condition, they may already be feeling a certain level of anger over the fact that they require medical intervention, so it is important that they are spoken to as young adults using an open, honest and practical approach. Throughout the clinical trial, it is important to speak to adolescents directly and answer any questions that they may have.

One Approach Will Not Fit All: Targeted Dissemination

Clinical trials involving children and adolescents are inherently more complex than those with adults, given the additional influence of family members, and, as children get older, of peers[5]. Healthcare professionals therefore need to understand the unique contributing factors affecting children and adolescents' ability to discuss and understand a clinical trial.

Young children (3-7 years old) require extensive parent involvement and support, especially when they are ill. Communication strategies for this age range should focus on positive reinforcement. For example, young children like to feel part of a club, so incorporating a token/reward-based system for adhering to the trial regimen may work well. Printed information should also be provided in a picture or storybook format, enabling them to interact and become part of the story. The focus here should be on an enjoyable, involving experience, ensuring the patient understands that other children are a part of the same club.

Pre-teens (8-12 years old) still require a strong involvement from their parents/caregivers; however, they should be

provided with additional information about the trial and what to expect. For example, if the trial requires an X-ray, what does the machine look like? Ensuring that this age group remains interested and motivated is key to ensuring their compliance and adherence. Printed information could also be provided in a comic book format, with a central relatable character explaining the trial to them in easy-to-understand language and corresponding visuals, helping to maintain their interest in the trial.

Adolescents (13-17 years old) have an increasing ability to understand health-related information, however, willingness to communicate with parents/caregivers and healthcare professionals may decrease during this age. The adolescent transition (e.g., puberty) involves a number of changes resulting in increased negative effect (e.g., anger, hostility, depression), heightened emotional reactivity and possibly decreased parental involvement. Adolescents need to feel that they are being understood and that the medical team can relate to them. Printed information could be provided in a magazine-style format to ensure it captures their attention, while still providing a clear understanding of the trial schedule and procedures.

Not all children develop at the same pace, and not all strategies will work equally well for each child. While printed materials, as outlined above, can be very effective communication tools, an important consideration related to paediatrics is that children learn and respond best to challenges through play. A key tactic to bringing play into paediatric clinical research is to make potentially unpleasant activities rewarding via online games, which is known as gamification.

Reaching your Target Audience: The Power of Play

The concept of gamification is rapidly developing within the healthcare industry. Initial research surrounding children and gaming focused predominately on negative consequences, such as increases in addiction, aggression, and anti-social behaviour[6-7]. More recently, however, games have been recognised as a powerful form of engagement and motivation and have been associated with significant improvements in the following health-related areas[8]:

- Disease self-management
- Health education
- Physical activity
- Psychological therapy outcomes
- Physical therapy outcomes

This approach can be very appealing to children and their caregivers, since play does not only take place in the park these days, but also online. Many young children are already very adept at using computers and hand-held devices, and this medium may be particularly promising for adolescents, who already spend large amounts of time online. There are benefits for all parties involved when fun and rewarding games are provided to support a child throughout a trial. Benefits may include increased compliance, responsibility, independence, and entertainment value:

Compliance:

Fighting with children to complete health-related activities that they find unpleasant or annoying is not uncommon (e.g., diary completion, medication adherence, diet and exercise). One of the biggest concerns study sites may have when conducting a trial with children is non-adherence, which can often be as high as 50 % among young patients with chronic condition[5, 9-10]. Through competition and reward, children gain self-management and self-efficacy (the belief in one's ability to achieve a specific goal). By associating unpleasant trial procedures with a game that is both interactive and rewarding, children will be more motivated to complete study assessments. This is especially important when it comes to clinical research, as children will be less likely to view trial activities as a burden and compliance will increase as a result.

Responsibility and Independence:

Games that promote learning will empower children to take responsibility for their health and manage their condition.

Many children go through the 'why' phase - 'Why this?' or 'Why that?' Providing children with background information about their disease, what actions they need to complete and the reasons why, will help ensure that they are on the right path to responsibly managing their condition from childhood to adulthood. In addition, children can often navigate the internet far more easily than their parents, at the risk of finding information not intended for a paediatric audience. By providing children with a safe online platform, games enable them to learn more about their illness in a secure and fun environment. Likewise, games can help children understand the importance, and consequences, of self-management strategies.

Entertainment:
Finally, it's fun! For those children and adolescents who may have spent a long time isolated and at home due to their illness, an online game gives them the ability to be more independent, and live a life outside of their illness. A game can allow them to immerse themselves in a world created for people just like them, that is both entertaining and captivating. Gamification allows sites to offer safe and controlled online communities where patients can connect with others.

Summary and Conclusions
Depending on the needs of the clinical trial and available budget, digital tactics alone may not be the answer. Sponsors and clinical research organisations (CROs) may wish to consider other formats that are targeted, yet flexible; for example, an online game that can be converted into a comic book. This is important to keep in mind during the planning process, especially in relation to global studies, where not all study populations will have access to smartphones or computers. Another important factor to consider during the planning process is that digital tactics often require a longer development time prior to implementation, and should therefore be considered for longer-term studies and/or those studies where data is required to be collected at home through patient-reported outcomes.

At the heart of a successful paediatric trial is clear communication with your target audience, which consists of a two-pronged approach:

- Sites engaging patients and their parents/caregivers
- Parents/caregivers supporting their child through this journey

A site's ability to engage children and their parents is key to ensuring successful trial recruitment and retention. Prior to the implementation of any paediatric trial, a thorough understanding of the target population should be in place. Sponsors and CROs need to know their audience in order to determine the best, developmentally appropriate, communication strategies. By planning ahead and looking at the paediatric population as distinct groups with distinct needs and motivations, trial teams can build targeted communication programmes to appeal to all age groups and their parents/caregivers.

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Shawn Patterson Baker is a Vice President at AXON Clinical Trial Services. With over 10 years' experience on global patient recruitment and retention programs, spanning 65 countries worldwide.
Email: s.pattersonbaker@axon-com.com

Jennifer Eastabrook is a Scientific Advisor at AXON Clinical Trial Services. Prior to this, Jennifer received her PhD in developmental psychology, where she researched emotional development across childhood and adolescence.
Email: j.eastabrook@axon-com.com