Children in Clinical Research: Parents and Children Share Their Needs, Challenges and Motivations for Participating in Clinical Trials

The pandemic has brought to the surface a host of long-standing challenges that the medical community at large is now seeking to address: Among them, how to increase clinical trial participation within our most vulnerable populations, whose representation in clinical trials is historically low?

Children comprise one of these key groups, and their lack of participation in trials has left gaps in our understanding of how medications affect children versus adults. Far from simply being small adults, children have unique developmental needs and physiologic responses that make it critical to evaluate drugs in the specific populations who will be using them. The risks, benefits and side-effects of drugs – as well as their impact on normal childhood growth and development – make it essential to expand paediatric participation in trials.

The Current State of Paediatric Research

The numbers of paediatric studies remain low around the world. Only 16.7 per cent of the total number of clinical trials registered on the World Health Organization's (WHO) portal involve paediatric patients, and only 12 per cent of trials registered on clinicaltrials.gov are paediatric trials, even though children contributed to almost 60 per cent of the total disease burden of the conditions being studied.[1]

The reasons for these numbers are vast and varied. Parents may be unfamiliar with clinical research, worried about the potential risks of an investigative drug, or concerned that their child could receive placebo instead of active drug. Their paediatricians may not be aware of local research studies and thus not suggest them as an option. Logistical barriers of work, travel, cost of transportation, childcare and sibling schedules may simply be too onerous to participate. Above all, our industry at large has not communicated broadly enough, and in practical terms, about the vital role of clinical research in developing newer, safer and more effective therapies.

So, what can the pharmaceutical industry do to more consistently engage families in joining paediatric clinical trials? The first step is to listen to patients and caregivers, to better understand their motivations, barriers and perceptions of clinical research.

Every two years, the Center for Information and Study on Clinical Research Participation (CISCRP) conducts a global study on public and patient perceptions of clinical research to monitor trends and identify opportunities to better inform and engage all stakeholders in the clinical research enterprise. In April, CISCRP conducted an online survey of 500 parents and children in the US about their attitudes and experiences regarding clinical trials. Some of the respondents had participated in clinical studies while others had not.

Altruistic Motivations

The survey findings were instructive and provided a window into nuanced, but meaningful, elements that could enhance children's participation in trials. Among them, altruism was a motivating factor for both parents and children. Sixty-three per cent of children

listed their primary motivation as the desire to help scientists learn more about their disease, and 42 per cent of parents listed altruism as their top motivation.

While altruism is often cited among adult trial participants, this selfless sentiment from children should provide renewed motivation to communicate the value of clinical research in recruitment and educational materials designed for kids.

In many respects, the pandemic has awakened the world to the importance of clinical research and, now that awareness is heightened, it is our duty to expand on that knowledge by changing how, how often, and to whom we communicate about clinical research.

The Child's Perspective

Little comforts can often make a big difference in how kids relate to an activity or task in front of them. Sixty per cent of children surveyed said that having free wi-fi at the site was very important, and 59 per cent of children said the availability of meals or snacks at study sites was also very important. Perhaps less expected was the importance of hearing from other children who had participated in research. Fifty-eight per cent of children surveyed said that "getting to hear from other kids like me" who have taken part in a study was a priority.

As the industry works toward increasing the patient voice and forming patient advisory councils to communicate patient preferences, it is important to consider the inclusion of younger ambassadors who, with their parents' permission, can share their experiences with other kids, either in person at a site, via videos, or through patient advocacy groups. Such a strategy could help alleviate one of the major barriers, that of fear, identified by children in the survey.

This is a key learning, because sixty-two per cent of children surveyed said their top barrier was that "something bad could happen or they would get more sick", a sentiment that speaks to the importance of educating children and demystifying the study process through personal accounts from other children.

Both parents and children should be included in clinical trial discussions so that questions and concerns can be adequately

addressed for both parties, ensuring a truly informed consent. Encouragingly, 92% of children remembered receiving information about the trial before joining, with only 15% finding it hard to understand the details.

Moreover, for kids who had previously participated in a trial, 90% said they would want to participate again, suggesting that it is often fear of the unknown – rather than actual trial elements – that inhibits participation.

Disruption to Daily Life

Patients and investigators have shared in the past the enormous challenges of having a child with a serious or rare disease. Joining a trial means taking time out to attend additional appointments, complete more forms and questionnaires, perform additional tests and take additional or new medications. Juggling these added tasks with work, family and siblings – or potentially flying or driving long distances to a study site (with associated financial limitations) – may present undue hardships.

The CISCRP survey showed that thirty-one per cent of parents whose child had participated in a clinical trial reported that it was "very disruptive" to their daily general routine, and 28% said it was "somewhat disruptive". Though specific study details were not included as part of the research, it would be useful to determine whether disease type or severity has any correlation to perceived study burden and exactly where those burdens are most severely felt.

The Role of the Paediatrician

Parents generally trust their paediatrician to be their first point of contact and to have their children's best interests at heart. Survey results showed that paediatricians play a vital role in both the parents' and children's decision-making processes about participating in a clinical trial. While parents cited advertisements as a common vehicle for hearing about a clinical trial, parents were most likely to cite a doctor's recommendation as the primary reason for enrolling their child.

With this insight in mind, it is critical that those conducting clinical trials provide comprehensive information and outreach to paediatricians. Paediatricians must be well-equipped to fully explain to families what they can expect from a trial, including all the potential risks and benefits, to fully inform parents and children about the process. Gaps in understanding can create undue stress and impede the ability to effectively manage their child's health problems.

Providing short study videos – designed for children of different ages and comprehension levels – can make complex information

much more clear and accessible. Additionally, telemedicine visits can make for convenient and private communication between researchers and participants, which encourages continued engagement throughout the trial.

Patient Advocacy and Patient Advisory Councils

How can the industry work toward reducing study barriers noted in the survey? At a strategic level, building strong relationships with paediatric advocacy groups and creating patient advisory councils can lead to overarching solutions to better support patients and caregivers across paediatric trials.

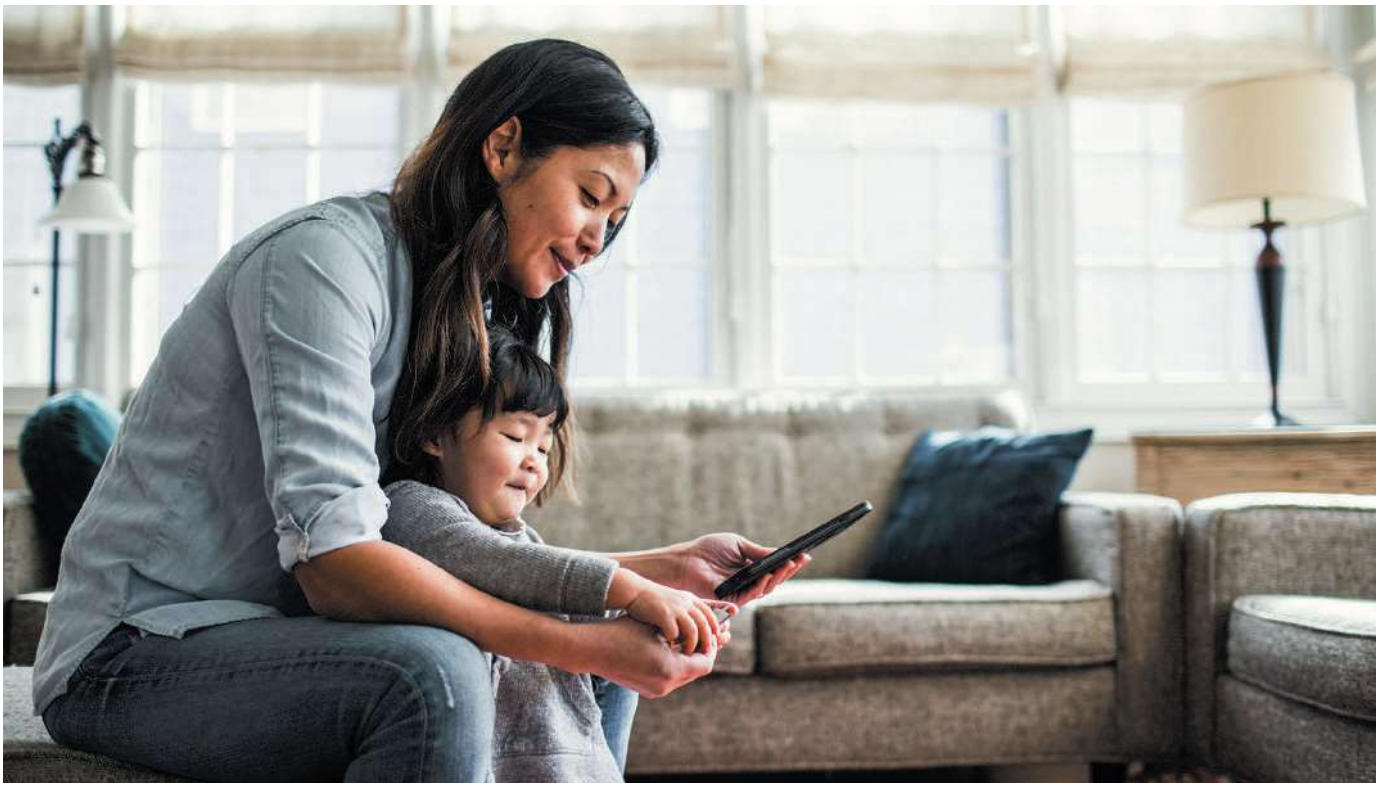
On a study-specific level, engaging parents in disease-specific trial designs can identify both medical and practical barriers up front. For example, in an asthma study for children, requiring children or teens to go to a clinic for a peak flow measurement on a weekday morning could prevent them from participating, whereas sending a home-health nurse could alleviate that seemingly small burden and make all the difference for families who might otherwise decline to participate. By understanding these challenges up front, the pharmaceutical company can adjust the protocol design early in the process or put into place practical support measures, or both.

The Rise of Decentralised Clinical Trials

The pandemic has clearly shown that we can and should make effective use of digital tools to communicate with patients and conduct study visits remotely using sensors, smartphone apps with telehealth and other technologies to ease the patient burden. Additionally, home-health visits and direct-to-patient drug shipments can further reduce site visits and enhance access to trial participation. Trials involving adolescents may be especially well-suited to using such tools, as teens are digital natives accustomed to communicating, learning and sharing data via devices. Decentralisation is particularly valuable in trials involving rare disease, since, by definition, patients are few and far between and thus will be spread over a wide geographical area where study sites are not easily accessible.

To be truly patient-centric, however, even a decentralised approach should allow for variations in families' needs and preferences. In such instances, participants may have the option to go into the study site or meet study personnel in a nearby hotel or community centre. On a recent decentralised trial with adolescents that required visits starting at 7 am to obtain 12-hour pharmacokinetic sampling, home visits were deployed to fit into teenagers' schedules rather than them requiring them to wake up exceptionally early for a clinic visit and potentially miss school.

Encouragingly, regulatory agencies around the world are increasingly accepting novel approaches to data collection and



remote monitoring in light of the pandemic due to the clear benefit to patients and the accuracy of data being collected.

Information is Key

Parents and children surveyed affirmed that knowledge is power: The more information they have, the greater sense of control they feel about the trial. Before deciding on whether to enrol their child in a clinical trial, 79% of parents said it would be "very important" to know the potential risks and benefits of the trial. Seventy-eight per cent said it would be very important to know the types of medical procedures required, and 73% said it would be very important to know the purpose of the trial and if their and/or their child's confidentiality would be protected.

A parent/patient advocate who participated in the survey stated that fear of the unknown was a key driver for her family in decision-making for her son Jack's treatments. "Rather than it being a reason for us not to participate, we used fear as a motivator to engage in research, find out about trials and bring them to the table with the medical team when they had appointments," said Rachel Daley, whose son has a rare disease called Langerhans Cell Histiocytosis.

"We always encouraged him to write everything down, and he'd take his journal into the doctor's appointments. I'd get my notepad out, and he'd get his notepad out as well. And we'd always do simple things like putting him in the seat near the doctor and be quiet until he'd had his chance to speak. I think that builds trust and instils confidence in children. It's really important to empower them to make those decisions and know that they're in control. I think Jack has felt informed and in charge of what's going on."

Creating a Seamless Experience

An overarching goal throughout all paediatric clinical trials should be making the process as straightforward and transparent as possible to simplify the lives of patients and their caregivers. Many of the practical challenges identified in the survey can be ameliorated through careful, personalised attention. For example, a patient navigator programme that provides support to parents or children can be hugely beneficial in assisting families with transportation challenges, insurance issues, educational materials, emotional support and more. In particular, patient navigators provide vital support to caregivers who might otherwise feel isolated or overwhelmed.

Drug developers, investigators and paediatricians must continually ask, how can we provide better information to families? How can we support them and improve their experience? How can we eliminate the trial barriers? How can we include patients in the discussion, as well as their parents, so that they also feel informed? As we emerge from the global pandemic, it is critical that we review, analyse and apply lessons learned to future clinical trials so the momentum we've gained is not lost. Most important of all, the greater awareness of clinical trials provides a critical opportunity for further educating the public about the vitally important role of clinical research.

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Rosamund Round

Rosamund Round, Vice President, Patient Innovation Center and Decentralized Trials at Parexel, collaborates with patients and customers to implement strategies that simplify the patient journey throughout clinical trials. Focused on reducing practical, financial and geographical barriers to study participation, Rosamund is excited by the industry shift toward a truly patient centric approach that incorporates decentralized clinical trial approaches to reduce the patient burden and increase access to trial participation.