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Global provider of eCOA and patient-centric solutions

Overcoming the Complexities of Pediatric Clinical Trials

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Although children make up 25% of the world's population, at least 50% of all drug products may still lack labeling with pediatric information. Drugs without proper clinical research in pediatric patients greatly raises the risk of unexpected adverse events: in 2008, 211,209 visits to the emergency room were by children 12 or younger due to adverse drug reactions.

The evolution in pediatric legislation,[1] a growing commitment to pediatric studies by the pharmaceutical industry, and a renewed interest in therapeutics for rare diseases have increased the demand for timely, high?quality, cost?effective clinical trials in children.[2,3]

However,

approximately one in every five pediatric clinical trials fail[4,5] . A 2016 study shows that over a three-year period (2008 -2011),
more than 77,500 children participated in studies that contributed little or
nothing to advance treatments for their illnesses because the research

disappeared from scientific view[6]: what
challenges cause these failures and how can they be overcome?

- 3 critical challenges of pediatric clinical studies

- 3 tips to overcome these complexities

- See the infography “Overcoming complexities in pediatric clinical studies“

3 critical challenges of pediatric clinical studies

Burden of Informed Consent

Informed consent for participation in pediatric clinical trials is very complex. In addition to the ethical challenges (ethics committee approval, capacity of the child to understand the value and the risks), the administrative procedure is cumbersome. Children may be asked to give their consent through an assent, depending on their age, and the assent information should be adapted accordingly.

A parental consent is also needed for a minor. In several countries, depending on the level of the risk, regulatory authorities require the consent to be given by both parents/legal guardians, which may be hard to obtain and adds time and complexity to the informed consent process.

As such, the whole informed consent process is very heavy and often quite long to manage, which has a negative impact on the enrollment process.

Small pool of patients

Not only is the informed process very complex but the pool of patients can be very limited in pediatric populations, and pediatric investigations face unique challenges. There simply are not as many children as adults (just 20 % of the U.S. population is younger than 14). Furthermore, children are, thankfully, less likely than adults to suffer serious illnesses.

> “So, by definition, most childhood diseases are rare,” says Danny Benjamin, a professor of pediatrics at the Duke University School of Medicine.[6]

And, last but not least, parents are skeptical.
The whole decision-making process is very different and critical in pediatric research. Children are more influenced by their relatives than most adults, and parents/legal guardians can show reluctancy to approve their child’s participation in trials. These misgivings can impact the child’s own appetite to join the clinical study, should the child be old enough to contribute to the decision. Also, the psychological impact of adding the burden of protocol procedures to the hardship that sick children are already going through is to be considered.

> “Recruiters generally don’t take enough time to understand the day-to-day circumstances and motivations of the populations they’re trying to enroll,” says Yvonne Joosten, director of one of the network’s newly funded programs at the Vanderbilt University Medical Center.

And so whichever the context of the pediatric trial set-up, the time required to get the sample size needed for the study can be extended when compared with adult trials. This has a significant impact on study timelines, which is paramount to successful pediatric clinical trials. The failure to respect the study milestones may have significant consequences: 40% of the trials conducted between 2008 and 2011 were never finished or finished but not published.[7]

Diversity of data providers

When it comes to providing the study data, pediatric patients may not be able to complete questionnaires or diary data themselves, and so different modes of data entry can be made available: Observer Reported Outcomes (ObsRO), when a relative provides the data, Clinician Reported Outcomes (ClinRO), when a health professional completes questionnaires, and Patient Reported Outcomes (PRO) or diaries when the patient him/herself provides the information.

This leads to data being captured in several modes, by different people and using potentially multiple devices. The diversity of users and devices has risks that can impact the quality of the data collected and that are to be considered upfront of study start.

In addition to the potential bias that can be introduced by the variety of questionnaire administration modes, the management of several users is not always obvious: technical and logistics problems can get multiplied, especially when young children are asked to complete questionnaires at home (e-diaries) and may forget their PIN code.

In some studies, diaries must be filled out several times a day over a long period of time, which is a daily burden and requires patients' time. Children might not see the value of doing that and can find the process boring in the long run.

On top of these issues, it's essential to guarantee the availability and the engagement of all participants to ensure everyone's compliance even more in this patient population that has already been so hard to enroll and where every single patient is irreplaceable.

3 tips to overcome these complexities

Securing compliance

Compliance stems from the commitment of site staff, parents/legal guardians and pediatric patients.

To make pediatric patients willing to provide data throughout the study, clinical trial stakeholders should turn to engaging playful designs. The questions must seem appealing; colors as well as animated images should be integrated. As an example, an animal that appears throughout the questionnaires, that speaks, reads questions (while the observer can still mute it), imitate symptoms and congratulates the child when the questionnaire is finished will help the child and his/her caregiver to fill in the questionnaire. Compliance can also be strengthened with instructions and videos to make questionnaire completion interactive.

The newest generation is more comfortable with advanced technologies than the older one, and it is expected that using electronic devices for clinical data collection will enhance compliance. Nevertheless, the electronic solution should be simultaneously appealing for pediatric patients and user-friendly for parents/legal guardians, who might be more reluctant to use new technologies, and the data collection solution should be designed as a helpful tool to ease their clinical trial experience.

Customizing training programs

Facilitating clinical trial experience starts with providing adapted training programs.

24/7
multilingual Help Desk & Initiation training calls, customized training by age group and adapted user facing text might be implemented in order to ensure the right level of understanding is achieved in each age category. Time spent on training will also have to be adapted, based on concentration abilities varying in the different age groups as well. The site staff’s resources may likely have to be adapted as well, so that customized explanations and dedicated demo sessions can be provided to the different age groups and to the parents’ populations.

Improving ability to provide data

As it comes
to the data capture itself, pediatric research has some specificities that need to be understood and anticipated. The informed consent process can be facilitated by an animated assent, or an image series can be used to be remembered more easily as PIN codes might not be suited for children for logging in.

To optimize
the quality of the data collected, every user has an individual secured access to his account and can log at any time and place. Immediate synchronization and data transmission are ensured to reduce the risk of data loss, and the audit trail allows traceability of who recorded the data and when, as well as all the complete history of data changes.

Even if
each clinical trial data provider has usually his own determined secure access and profile, there might be a need to create a “mixed” profile between ObsRo & PRO profiles. Such a feature would allow questionnaires to be completed by a parent or caregiver when the patient is not able or willing to fill out a given session that was set up as a PRO. As a facilitator of the day-to-day patients’ life and being adapted to real life constraints, it would both improve ability to provide data and enhance compliance.

For
long-term studies, we need to rethink the way we engage children and secure

data provision for long periods of time. Innovation seems to be key to keep patients engaged and ensure compliance in the long run. Goal-oriented games can be used for both training programs and data collection to make the clinical trial's experience more user-friendly. Also, virtual rewards or medals can be integrated to increase children's motivation and to value the importance of their participation in the trial.

Although a lot of initiatives have been taken to develop pediatric research, challenges must still be faced to secure the success of pediatrics studies. Compliance remains a critical challenge for the success of the study but guaranteeing the recruitment target is undoubtedly the first critical step. The development of new digital technologies should ease the informed consent process, help improve and monitor patient compliance and provide a promising alternative to simplify data collection and offer greater flexibility to the participants.

Project Managers @Kayentis

KAYENTIS EXPERTISE

1/ User friendly solutions for all
data providers, and possibility to centralize data collection on a single
device

> **A solution that simplifies data collection**

2/ Capability to integrate an eICF solution App
in the same device, that offers an easy-to-understand consent form, with audio
of the approved consent in the patient's language and embedded information for
specified concepts

> **A solution that integrates informed consent process**

3) Customized design and layout, in
order to adapt to the therapeutic area, the specifics of the patient age, the
study duration and the study budget. Capability to integrate videos and graphic
designs to adapt to for pediatric population

> **A solution that improves patients' and care giver's compliance**

See "How can digital innovation turn clinical trials into a positive patient and site experience?":

Click here

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