Data and digital tools in pediatric clinical trials
Decentralized Clinical Trials
The Future of Medical Product Development

T he COVID-19 pandemic changed many clinical trials that were previously bringing new therapies to market on an additional onslaught of the pandemic in terms and quality of life owing to delays in enrolling potentially benefitting patients. In this effect, the pandemic has seen the adoption of remote interactions between investigators and patients to provide continuity of care while maintaining social distancing. This creates a time of rapid advances.

Currently, clinical trials for drug approval often already include decentralized elements, and DCTs often incorporate traditional design with decentralized methods at the previous/post intervention clinical trials.

ADVANTAGES OF DCTs:
- SMALLER, FEATTER, CHEAPER, MORE DIVERSE
- DCTs may improve the logistics of conducting a

In the wake of COVID-19, decentralized clinical trials move to center stage

Marc A. Bales, Science Writer

In January 2021, New York’s Northeast Health hospital system launched a clinical trial to test whether the anti-inflammatory drug Remdesivir, also known as Remd, reduced the severity of COVID-19 in symptomatic patients, who do not require hospitalization. The clinical trial was designed to enroll up to 500 patients and evaluate the safety and efficacy of Remdesivir in reducing COVID-19 health outcomes. The trial, which Northeast Health conducted in partnership with the Cold Spring Harbor Laboratory, NY, has concluded enrollment as of September 2021. Data analysis is ongoing.

Northeast is not the only one seeking volunteers for clinical trials, and the pandemic has led to a surge in interest in these types of studies. The availability of vaccines made it easier for patients to participate in clinical trials, as they were less likely to be hospitalised or experience severe symptoms. This led to increased participation and awareness of clinical trials, which has been a positive outcome of the pandemic for the healthcare industry.
‘Opportunities provided by the digital environment play an increasingly crucial role in children’s development and may be vital for children’s life and survival’

Children reported that the digital environment afforded them crucial opportunities for their voices to be heard in matters that affected them’

‘..decentralised measures should improve the efficiency of future paediatric clinical trials...sponsors can reduce the trial burden to children and their families by incorporating flexibility in timing and number of hospital visits. This is important as missing school or social activities is one of the main self-reported burdens to children when participating in trials

United Nations Committee on the Rights of the Child, General Comment 25

Improving clinical paediatric research and learning from COVID-19: recommendations by the Conect4Children expert advice group
Patient reported outcome assessment must be inclusive and equitable

Patient-reported outcomes are increasingly collected in clinical trials and in routine clinical practice, but strategies must be taken to include underserved groups to avoid increasing health disparities.


Patient-reported outcomes (PROs) collected in clinical trials can provide valuable evidence of the risks and benefits of treatment from a patient perspective, to inform regulatory approvals, clinical guidelines and health policy. PROs are increasingly collected routinely in clinical settings, at an aggregate level for audit and benchmarking, for real-world evidence generation, and as an input or predicted output for clinical decision tools and artificial intelligence (AI) in health. At an individual patient level, PROs can be used to facilitate shared decision making, screen or monitor symptoms, and provide timely care tailored to individual needs. PROs are also increasingly used in value-based healthcare initiatives.

Efforts to capture and report PRO data should be inclusive and equitable, addressing the diverse needs of all patients with the condition of interest, including groups historically and currently underserved by research. Issues of diversity, equity and inclusion (Box 1) have recently been highlighted in PRO ethical guidelines, which have identified a number of concerns to be addressed in PRO research.
What We Do

Aparito brings clinical trials to patients and unlocks real-world data through mobile apps, video assessments & wearable devices.

We provide a patient-centric platform that integrates clinical & regulatory expertise to capture patient data and develop digital endpoints for hybrid and decentralized clinical trials to streamline the drug development process.

We digitize clinical trials.
Atom5™ Features

Atom5™ is the clinical trial platform that offers Video Assessments, PROs, Telemedicine, EDC and eConsent.

All via one smartphone app.

- Patient App & Dashboard
- Clinical & Sponsor Portal
- eCOA
- Data Analytics
- Regulatory Compliance
Patient App & Dashboard

Self Onboarding and eConsent
Patients can be onboarded and consent to the study remotely from their dashboard.

Questionnaires
Customized or clinically valid digitized PROs

Tasks/Assessments
Allow patients to carry out assessments and perform task from the comfort of their home.

Tasks & Assessments
Patients can perform tasks from the comfort of their home including our vTUG and SARAhome video assessments.

Diaries
Allows patients to report a range of information from symptoms to medication dosage that are taking.

Events
Allow patients to report adverse side effects in real-time.

DocuSign* partnership allows FDA compliant consent.
Video
Atom5™ video capture & analysis locates specific points on the body and computes the speed and trajectory of each movement to explore smoothness of motion and erratic patterns, enabling clinicians to assess features such as gait and posture.

ePRO
The PRO module is fully configurable and tracks actual patient outcome scores in addition to measuring each patient against the cohort. Our technology also has personalized branching for response-based data capture, making data capture more dynamic.
Atom5™ Unique Offerings

**SARA**
The SARA tests were digitized as SARA**home** in collaboration with DZNE.

SARA**home** and conventional SARA are highly correlated.

**vTUG**
The video timed up-and-go (vTUG) test uses video capture and pattern recognition to enable objective, sensitive high frequency assessments.

**FEEDS**
Feeding & Eating Evaluation viDeo analysiS (FEEDS) uses Atom5™ software to identify specific points on the face and hands and apply machine learning techniques to characterize age-dependent eating skill and technique.
Clinical & Sponsor Portal

Clinician Portal
This allows the clinician to upload clinical data to the system, and communicate directly with individual patients

Real-Time
All patient captured data can be viewed in real-time to ensure quality and regular uploads

Dashboard
This allows the sponsor to view all patient data in an individual or cohort view with controlled access to the eCRF and eTMF

Verification With e-Link
PI can issue a specific link to the patient via their email which they need to access the e-consent
Patient Group Accelerator Programme
Patient Group Accelerator Programme

The Aparito Patient Group Accelerator Programme (Accelerator) addresses the high unmet needs of patient communities by co-developing new digital biomarkers with patient groups.

Aparito launched the Accelerator programme in 2020 to provide an initiative where a company and patient community, with the support of patient advocacy groups, can collaborate as peers.

The Accelerator is designed to understand and ideally fulfil the patients’ needs, by working closely with patient organisations and finding new endpoints that would be relevant to their specific conditions.

Aparito has a long-standing expertise in working with patient groups and won the EURORDIS Black Pearl Award 2022 for Health Technology!
DMDHome Co-Creation Pathway

Location: UK
Condition: Duchenne Muscular Dystrophy
Duration: 12 Months

Overview and Challenges

Aparito worked with Duchenne UK to identify new digital biomarkers that could help provide a more accurate mapping of the transfer stage of the disease, i.e., progression from ambulatory to non-ambulatory, and that focused on upper limb strength, which was identified as important for patients in all stages of DMD.

Participants were put into cohorts to ensure that they weren’t asked to complete a task which they were physically unable to do.

- Cohort one: ambulatory
- Cohort two: transfer
- Cohort three: non-ambulatory

Our Approach

12 participants onboarded to app
Total of 62 videos uploaded, from 8 participants
52 videos (84%) used in analysis (remaining do not include task, or completed task)
Pose Estimation Software

**OpenPose**
Open-source software that detects points on the human body, hands and feet. Output is a json file per frame, with pixel coordinates of each body point, and a confidence value associated with each point.

**MediaPipe**
Open-source framework for creating machine learning projects that analyse video data. Many additional computer vision tools to pose-estimation e.g. segmentation, tracking.

github.com/CMU-Perceptual-Computing-Lab/openpose
openpose software

- **OpenPose** is open-source software that detects points on the human body, face, hands and feet.
- Can detect multiple people, or can restrict to specified number.
- Two different models – COCO (18pts) and Body_25 (25pts, includes feet).
- Output is a json file per frame, with pixel coordinates of each body point, and a confidence value associated with each point.
- Optional additional output is a copy of the original video, annotated with the identified body points.
Time to See the Difference: Video Capture for Patient-Centered Clinical Trials

Elin Haf Davies\textsuperscript{2,3} - Clare Matthews\textsuperscript{2} - Adeline Merlet\textsuperscript{4} - Martine Zimmermann\textsuperscript{1}

Accepted: 12 December 2021
© The Author(s) 2022

Abstract
Developing therapeutics for the treatment of rare diseases usually requires a strong understanding of the natural history of the disease. Often, it also requires the creation of novel assessment tools and clinical trial endpoints. In diseases where mobility is impacted, the use of video to capture the impact of the disease and the assessment of specific parameters, such as gait and stride length, can help design sensitive endpoints. Video as an assessment tool also allows the use of historical videos or videos filmed by non-experts outside of clinical settings. Given the increased use of telemedicine, the use of video may be a useful addition to clinical trial assessments. Two cases are presented: (1) the use of video in the development of asotase alfa (Strensiq\textsuperscript{®}) in hypophosphatasia is detailed as an example of the utility of this type of assessment in rare diseases; and (2) a home-setting video tool that was developed and validated (SARA\textsuperscript{TM}) from a commonly used clinical scale (Scale for the Assessment and Rating of Ataxia [SARA]), allowing patients to record their own severity of ataxia. While there are certain limitations associated with video assessment, advancing technologies such as automated analysis and machine learning provide a tremendous opportunity for automated analysis of video recordings, reducing the bias associated with human assessment.

1 Introduction

...
m-Health in the management of paediatric epilepsy
Medication Adherence in Practice

Medication Adherence as Observed Across a Pediatric Epilepsy Cohort within a Resource-Limited Setting

- Patients with a diagnosis of “refractory epilepsy” aged between 4-15 years (median: 10) were recruited for the study.
- Patients were required to download the study specific smartphone app powered by the Atom5™ software platform.
- **Influencing and monitoring adherence:**
  - Prompts were provided for patients when their antiseizure medication (ASM) was due.
  - Caregivers were able to state whether medication was taken or not, and provide reasoning.
  - A medication adherence report was also completed in addition.

aparito
Medication Adherence in Practice

Medication Adherence as Observed Across a Pediatric Epilepsy Cohort within a Resource-Limited Setting

"Yes, sometimes I do forget to give him (the medication)"

"I found the phone very helpful. It was reminding me when it was time for meds"

That is helpful because you can just capture events every day and you don't have to remember everything when you go for follow-ups"

Reasons for non-adherence encompassed:
1. Forgetfulness (the most common factor)
2. Self perceived inefficacy (drug does not work)
3. No remaining drugs
4. The belief that it was making their child unwell (side effects)

Demonstrating the feasibility of digital health to support pediatric patients in South Africa

A qualitative study exploring caregivers’ experiences, perspectives, and expectations for precision medicine in epilepsy in South Africa
Epilepsy & Behavior Volume 117, April 2021,
A qualitative study exploring caregivers’ experiences, perspectives, and expectations for precision medicine in epilepsy in South Africa

Irene Farisal Muchada 1,*, Jo M. Wilmshurst 1, Nakita Laing 2, Elin Haf Davies 3, Karen Fieggen 4

1 Division of Human Genetics and Department of Medicine, University of Cape Town, South Africa
2 Pediatric Neurology Department, Red Cross War Memorial Children’s Hospital, Neuroscience Institute, University of Cape Town, South Africa
3 Aparito Health, United Kingdom

ABSTRACT

Purpose: Successful implementation of innovative Precision Medicine initiatives in the management of children with complex epilepsy is largely dependent on the caregivers’ engagement with the technology as well as its accessibility and acceptability. We investigated the feasibility of implementing these initiatives in the South African setting by gathering information on the caregivers’ experiences, perspectives, and expectations for Precision Management of Epilepsy (PME) initiatives.

Methods: We purposively recruited 12 participants from a cohort of 40 caregivers of children with complex epilepsy recruited for a PME study attending Red Cross War Memorial Children’s Hospital (RCWMCH) in Cape Town, South Africa. Face-to-face semi-structured interviews were conducted using a pragmatic qualitative approach and themes were extracted using a thematic framework approach. Results: All participants had ideas about the cause of epilepsy, but many did not think that epilepsy is a medical condition. There were several difficulties in adhering to medical treatment which was sometimes combined with traditional remedies and practices. Understanding of Precision Medicine in the context of research was limited and although participants were uncertain about benefits, most were optimistic about the future. Mobile health devices introduced new feelings and challenges for many participants. The four themes which emerged were: (1) Cause of epilepsy: uncertainty and conflicting views; (2) Need for helping; (3) PME mobile health devices; and (4) Feasibility of implementation of PME initiatives.

Conclusion: For Precision Medicine to be widely accepted and beneficial, how people understand the cause of epilepsy, difficulties in adhering to treatment, and personal experiences need to be addressed.

© 2021 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license [http://creativecommons.org/licenses/by-nc-nd/4.0/].

Demonstrating the feasibility of digital health to support pediatric patients in South Africa

Elin Haf Davies 1 | Karen Fieggen 2 | Jo Wilmshurst 2 | Obuchineza Anyanwu 3 | Richard Joseph Burman 3 | Sandra Komarzynski 1

1 Aparito Ltd, Wrexham, UK
2 Division of Human Genetics, Department of Medicine, University of Cape Town, Observatory, South Africa
3 Department of Paediatric Neurology, Red Cross War Memorial Children’s Hospital, Neuroscience Institute, University of Cape Town, Cape Town, South Africa

Correspondence
Sanths Komarzynski, Aparito Limited, Unit 11-12 Dewars, Technology Park, Coveredway Rd, Wrexham LL13 7YF, UK.
Email: sanths.komarzynski@aparito.com

Finding Information
South African Medical Research Council; Newton Fund

Abstract

Objective: Resources for management of epilepsy in Africa are extremely limited reinforcing the need to develop innovative strategies for optimizing care. Studies have shown that the prevalence of epilepsy in low- and middle-income countries is substantially greater than in more resourced countries. The objective of this report was to demonstrate that mobile Health (mHealth) technologies have the potential to improve the management of epilepsy in Africa.

Methods: The feasibility of technology-based home monitoring was investigated in an observational study of 40 children with refractory epilepsy or epilepsy associated with intellectual disability and/or behavior difficulties in South Africa. Technology-based home monitoring was implemented for six months. Physical activity, sleep, and heart rate were continuously monitored with a wearable device. Caregivers completed regular mobile Patient Reported Outcomes (mPROs) and reported seizures and ad hoc events using a dedicated app. Feasibility was assessed and descriptively
Final points....
These ultrasound stickers can see inside the body

Aparito
Rhian.Thomas-turner@wales.nhs.uk