Measuring What Matters with eCOAs: A New Era of Patient-Led Innovation

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Introduction

Traditional methods for collecting Clinical Outcome Assessments have been transformed by technology, leading to the development of electronic Clinical Outcome Assessments (eCOAs).

COAs refer to clinical tests that assess how patients function or feel.[1] Due to their digital nature, eCOAs hold a variety of benefits, including capturing data electronically, minimising administrative burden, reducing time for patients required to go to healthcare centres and, importantly, increasing patient engagement.[2]

eCOAs also extend the accessibility and convenience of participating in clinical trials to patients who might be geographically isolated or have mobility constraints, thereby widening the pool of potential participants and facilitating more inclusive research studies.[3]

Background

Digital health technologies (DHTs) have become more prevalent and as a result, the digitisation from in-clinic to electronic versions of clinical assessments has enabled patients to conduct the tasks at home.

eCOAs open up the possibility to explore real-world scenarios and gather richer, more representative data, especially powerful tools to monitor conditions with a high degree of variability such as ataxia.

The U.S. Food and Drug Administration's paper "FDA Guidance on Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments: Old Wine in a New Bottle?" discusses the FDA's guidance on developing or modifying fit-for-purpose Clinical Outcome Assessments (COAs), emphasises the transition from patient-reported outcomes (PROs) to a broader range of COAs.[4]

In particular, the article delves into the evolving landscape of Clinical Outcome Assessments (COAs) within the pharmaceutical realm, as guided by the FDA's latest directives. It is a journey from the traditional patient-reported outcomes to a broader, more inclusive horizon that embraces a variety of COAs.

This shift is not just about methods; the narrative is one of embracing technology and a more patient-centred approach to drug development, challenging researchers to adopt more rigorous, evidence-based practices.

eCOAs offer improved data quality through direct capture from the source, real-time data access for quicker decision-making, enhanced patient engagement with user-friendly interfaces, increased operational efficiency by automating data collection, and global reach and accessibility for collecting data from diverse geographic locations.[5]

This transformation promises to reshape our understanding and measurement of treatment impacts, making it a pivotal moment for the industry.

Classifying COAs

COAs are classified into four categories (Figure 1): (1) patient-reported outcome assessments (PROs), (2) Clinician-reported outcome assessments (ClinROs), (3) Observer-reported outcome assessments (ObsROs) and (4) performance-based outcome assessments (PerfOs).

PROs

PROs are direct reports from patients about their health condition without any interpretation by healthcare professionals, covering aspects like symptoms, quality of life, and daily function.[6]

Electronic PROs (ePROs) empower patients to respond to document their health status using devices like smartphones or tablets. These outcomes encompass a patient's description of their symptoms and the impact of a disease or treatment on various aspects of their well-being.

Examples include the EQ-5D-5L and the Symptom Burden Questionnaire™ for Long COVID (SBQ-LC).

ClinROs

ClinROs are assessments made by healthcare professionals based on their observations and judgments, focusing on clinical signs, disease severity, and treatment response.[7]

Also known as PhysicianROs, they involve trained healthcare professionals who observe and interpret signs or behaviours related to a patient's disease or condition.[8] These reports must be compliant with regulatory frameworks and provide insights into observable aspects of a patient's health.[9] They are useful for assessing treatment efficacy and safety.

Examples include DMDhome, the Unified Parkinson's Disease Rating Scale (UPDRS) and the Modified Ashworth scale.

ObsROs

ObsROs are eCOAs reported by non-professionals, such as parents or caregivers, especially when the patient cannot report for themselves.[10] These assessments capture observable signs, events, or behaviours related to the patient's health condition, without including the symptom implications.

ObsROs are particularly relevant when patients themselves cannot directly report their experiences.

Examples include SARAhome and Seizure Diaries.

PerfOs

PerfO assessments involve standardised tasks that patients perform. PerfOs involve objective tests or tasks performed by the patient, measured and recorded by an assessor or an electronic system.[1] These tasks are well-defined and repeatable.

Examples include video Hand Opening Time (vHOT), 6-Minute Walk Test, and video Timed Up-and-Go (vTUG).

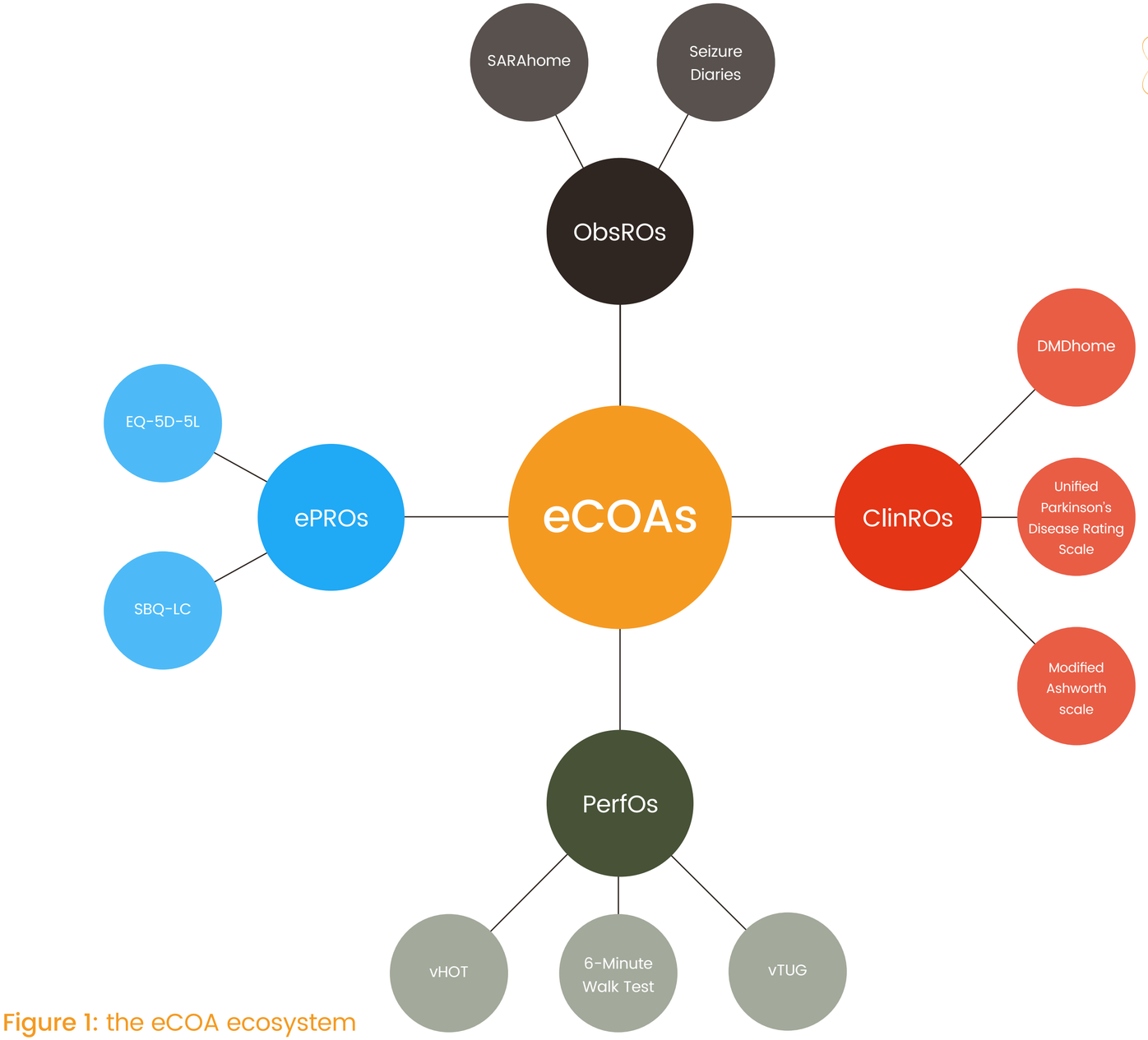


Figure 1: the eCOA ecosystem

The Myriad Benefits of eCOAs

eCOAs offer numerous benefits:

Enhanced Data Quality and Accessibility:

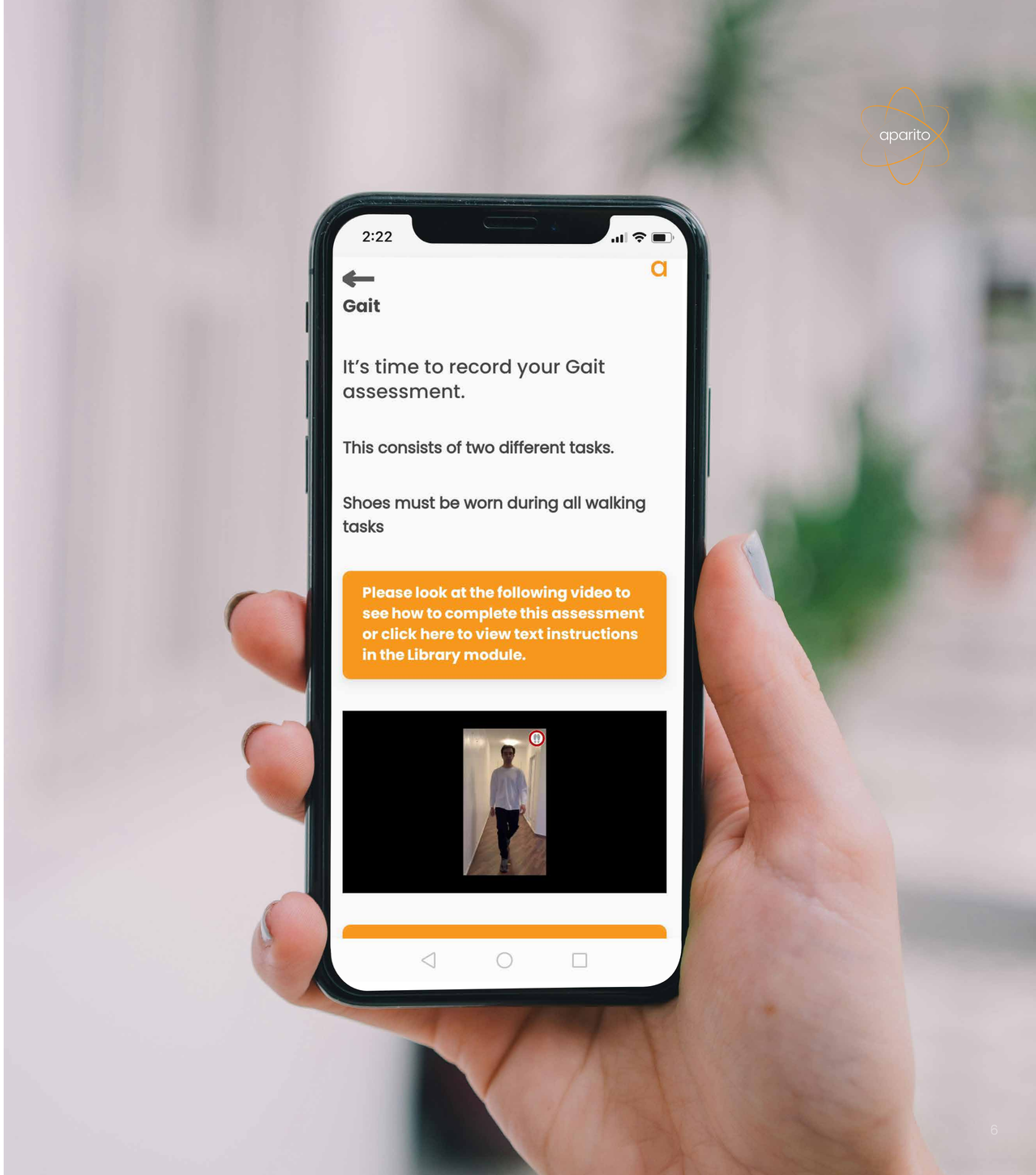
eCOA improves the accuracy and reliability of data collected by minimising human error. Electronic systems allow for immediate data entry, reducing discrepancies and enabling quicker access for data analysis.

Patient Engagement and Compliance:

The use of electronic devices (particularly a BYOD approach) makes it easier for patients to report outcomes, potentially increasing engagement and compliance. eCOA can facilitate more frequent and timely data collection, capturing patient experiences more effectively.

Operational Efficiency:

eCOA streamlines the data collection process, reducing the burden on both patients and clinicians. It can lead to cost savings by minimising the need for physical documents and reducing site visits, but the most prevalent cost savings are in better data quality from improved patient engagement and compliance.



The Myriad Benefits of eCOAs

Global Reach and Scalability:

eCOA systems can be deployed across multiple sites and countries, allowing for larger and more diverse studies.

Additionally, eCOAs are an emerging tool to measure activities of daily living (ADLs) outside clinical environments.

There are various reasons for collecting ADLs through eCOAs such as,

1) ADLs can capture fundamental skills such as speech and comprehension of instructions.

2) ADLs can help stakeholders obtain indications of a person's functional status such as eating and walking abilities.

3) ADLs can be expanded with electronic questionnaires, providing insight into patients' quality of life.

Digital clinical endpoints or concepts of interest (COIs) are important components of a clinical assessment to evaluate a patient's changing situation over a clinical trial. This can be compared to laying puzzle pieces that together form an entire puzzle.

Similarly, COIs should fit together in an eCOA to have the correct structure of event sequences e.g., one such COI could be the changes over time in distance walked (6-minute walk distance) during the 6-Minute Walk Test (6MWT). [12]

Digitising eCOAs

At Aparito we operate on two different approaches to digitising eCOAs;

1. Digitising an existing COA

2. Developing novel eCOAs

Over the next four pages, we'll show you how we do it.

Digitising an existing COA

In other scenarios, there might be an interest in digitising and simplifying an existing COA against a gold standard test [13] (Figure 2).

In this case, a conceptual framework must be selected and identified, to decide which DHTs will be applied in the digitised eCOA e.g., if video, wearables or electronic questionnaires will be involved.

For example, SARAhome is a video-based eCOA developed by condensing the eight domains of the Severity Ataxia Rating Assessment (SARA) scale performed in hospitals by clinicians to five domains completed by patients themselves at home. [14]

Based on the feasibility of self-application, five SARA items were selected (gait, stance, speech, nose-finger test, fast alternating hand movements) for SARAhome. The SARAhome items were compared with total SARA scores in 526 patients with spinocerebellar ataxia types 1, 2, 3, and 6 from the EUROSCA natural history study. [15]

To prospectively validate the SARAhome, the self-applied SARAhome was compared with the conventional SARA in 50 ataxia patients and to demonstrate the feasibility of independent home recordings in a pilot study, 12 ataxia patients were instructed to obtain a video each morning and evening over 14 days.

The outcome was significant: an average SARAhome score from five days of assessments provides a more meaningful measure and severity of ataxia than a conventional snapshot visit conducted once a year.

Atom5™

Atom5™ is Aparito's eCOA platform which supports hybrid and decentralised clinical trials with assessments at scale and has transformed clinical trials for sponsors and clinicians worldwide.

Atom5™ is 21 CFR Part 11, GDPR and HIPPA compliant and provides ePROs, video eCOAs, wearable integration, Telemedicine and eConsent in 193 countries and 125 languages.

Atom5™ generates continuous real-world data supported by a data science team that enhances data analysis using computer vision, image & signal processing, time series analyses and Machine Learning (ML) tools.

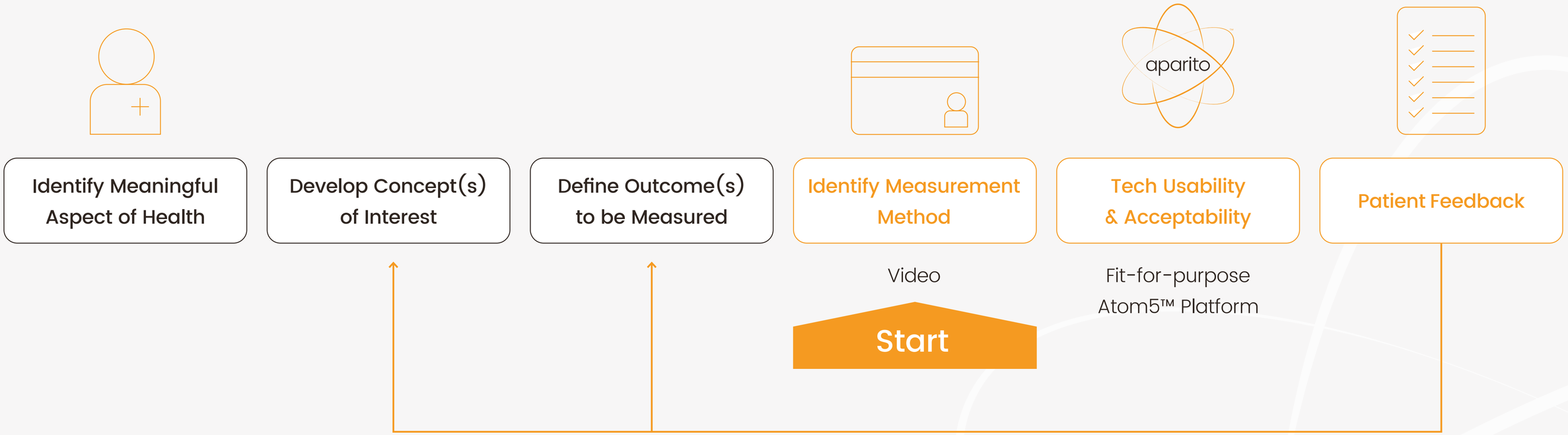


Figure 2: Digitising an existing COA.

Developing novel eCOAs

Current COAs or clinical endpoints may not capture a concept of interest (COI) that is relevant to patients (Figure 3). In this scenario, a new eCOA needs to be developed from scratch.

Such is the case for DMDhome, designed to detect disease progression from the late ambulatory to transfer stage and early non-ambulatory stage in Duchenne Muscular Dystrophy (DMD). DMDhome was developed following Duchenne UK being chosen to join Aparito's Patient Group Accelerator Programme to devise a patient-centred eCOA that was able to capture changes in functional ability and the associated impact on daily activities and quality of life.

Different tasks in DMDhome were developed and standardised for video capture. [16] The tasks were

1) Hands-to-head while standing

2) Hands-to-head while sitting

3) Sit-to-stand then hands-to-head while standing

By leveraging Aparito's video capture and computer vision analysis, this approach not only enhances the accuracy and accessibility of assessments but can also provide valuable insights into disease progression and treatment efficacy.

Early participant feedback provided a means to evaluate how user-friendly the new video-based eCOA is, which is crucial to assess user acceptance testing (UAT) and "usability validation before embarking on a validation study to address analytical and clinical validation as required for the V3+. [17]

Currently underway, the fully decentralised validation study measures how DMDhome compares to the current gold standard assessments such as the North Star Ambulatory Assessment (NSAA) and the Performance of the Upper Limb (PUL2.0) performed by a physiotherapist in the home environment. [18]

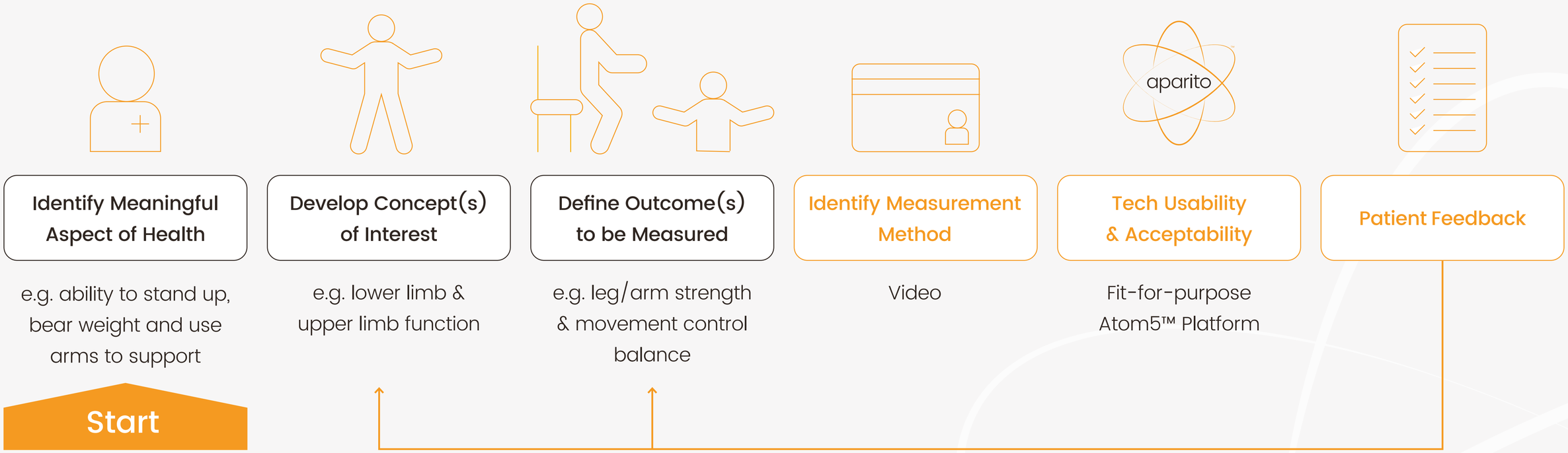


Figure 3: Developing novel eCOAs

Pushing the boundaries of eCOA

The potential for eCOA is boundless and developing use cases is a challenge we eagerly meet. Drawing on the concept of measuring what matters to patients and providing more insight into natural behaviours, we used our video Clinical Outcome Assessment (vCOA) capture and analysis capabilities to develop Feeding & Eating Evaluation viDeo analysiS (FEEDS) to evaluate the usability of parent/ caregiver captured videos of children's feeding and eating skills for clinical assessment.[19]

Our FEEDS study[20] explored dysphagia in children and highlighted how decentralised clinical assessments of paediatric feeding, (via smartphone video recording) offered a more natural environment for the child, reduced the family burden and provided an insight into a child's feeding behaviour not seen in a clinical setting.

FEEDS utilises the Atom5™ eCOA platform to

1) Identify specific points on the face and hands

2) Apply machine learning techniques to characterise age-dependent eating skills and techniques

3) Analyse chewing and swallowing coordination

Example measures include "time taken for plate-to-mouth action" (or alternative gestures) and "number of mouthfuls per minute".

This is one example of how vCOA can be used to transform how we think about COA development and the possibilities of what we can measure that are meaningful to patients and valuable to sponsors.

Conclusion

The adoption of eCOAs marks a significant shift in the landscape of clinical trials and patient care. This paper has underscored the transformative potential of eCOAs across various domains, emphasising their role in enhancing data quality, patient engagement, and clinical trial operational efficiency.

The transition from traditional paper-based assessments to electronic formats not only streamlines data collection processes but also extends the reach of clinical trials to a more diverse and inclusive patient population. eCOAs enable real-time data capture, facilitating quicker decision-making and providing a more comprehensive understanding of patient outcomes in real-world settings.

Moreover, the categorisation of eCOAs into PROs, ClinROs, ObsROs and PerfOs underscores the versatility and applicability of electronic assessments across different contexts and stakeholders.

The development of novel eCOAs and the digitisation of existing assessments offer tailored solutions to address specific research questions and clinical needs. Whether it's capturing subtle changes in disease progression or monitoring treatment efficacy over time, eCOAs provide a nuanced understanding of patient experiences and functional abilities.

Furthermore, the examples of SARAhome and DMDhome presented in this paper illustrate the iterative process of eCOA development, involving stakeholder engagement, usability testing, and validation studies. These efforts are essential not only for ensuring the reliability and validity of electronic assessments but also for fostering user acceptance and adoption in clinical practice.

The widespread adoption of eCOAs holds the promise of revolutionising clinical research and patient care. By harnessing the power of DHTs, researchers and healthcare providers can collect richer data, engage patients more effectively, and ultimately improve health outcomes across diverse populations.

In conclusion, eCOAs represent a transformative approach to clinical assessments, offering numerous benefits in terms of data quality, patient engagement, and operational efficiency. As the field continues to evolve, embracing electronic assessments will be crucial for advancing precision medicine, enhancing patient-centred care, and driving innovation in clinical trial operations.

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