Digital Endpoints: Enhancing our understanding of the patient experience

June 2022
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Today’s presenters

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Today’s agenda

+ Potential of digital health tools to better understand patients experience
+ Digital endpoints landscape
+ Difference between digital clinical outcome assessments and digital biomarkers
+ Guidance from regulators and payers
+ Strategies to realise the potential of digital endpoints
Digital Health Tools (DHTs) are key enablers for patient centricity, and have vast applications.

**We focus here on the digital medicine definition**

**Digital Health Technologies**

- **Definition**: Technologies, platforms, and systems that engage consumers for lifestyle, wellness, and health-related purposes.
- **Product Examples**: Lifestyle apps, fitness trackers, EMR systems, patient portals.

**Digital Medicine**

- **Definition**: Evidence-based software and/or hardware products that measures and/or intervene in the service of human health.
- **Product Examples**: eCOA, PerfO actigraph app, ecological momentary assessment, digital biomarkers.

**Digital Therapeutics**

- **Definition**: Evidence-based therapeutic interventions to prevent, manage, or treat a medical disorder or disease.
- **Product Examples**: Digital cognitive behavioral therapies in many different areas.

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Source: Figure from IQVIA MedTech

IQVIA | Digital Endpoints Webinar June 2022
Patients are best positioned to provide a real-world understanding of their disease and treatment experiences

“Patient experience data can be interpreted as information that captures patients’ experiences, perspectives, needs, and priorities related (but not limited to)

1. Symptoms of their condition and natural history
2. Impact of the conditions on functioning and quality of life
3. Experiences with treatment
4. Input from patients on which outcomes are important to them
5. Patient preferences for outcomes and treatments
6. The relative importance of any issue as defined by patients”

FDA provides a comprehensive definition of Patient Experience Data with acknowledgement of the importance of

- Generating reliable and valid data
- Ensuring interpretable outcomes
- Comprehensively understanding both benefits (efficacy) and risks/harms (safety) to inform decision-making

The EMA’s ‘Regulatory Science Strategy to 2025’ indicates that Europe is thinking in the same way - proposed that the core recommendation is expanded to “Ensuring the patient voice is systematically incorporated throughout drug development & associated evidence generation”

COAs in Oncology: Industry trends, Guidance and Implications
IQVIA Seminar: Complementing our understanding of patient experience with the use of digital tools | June 2022
DHTs have many benefits, allowing capture of patient experience data and helping us better understand how patients feel and function.

**Continuous measurement and monitoring**
- Understand variability that can arise from continuous measurements, in comparison to single timepoint assessments
- Explore trends within days, as well as between days

**Longitudinal individual-level data collection**
- Active and passive capture and low burden on patients
- Measure changes over time, and establish events sequencing

**Enhanced understanding of patient experience**
- Broad and deep view into patient functioning
- Patient experience in real-world setting
Many pharma sponsors have started exploring collection of digital endpoints in clinical trials, mainly as primary and secondary endpoints.

*Only drug trials with reported phases are included

In the last two years, the number of digital endpoints included in clinical trials has increased ~ 4x between 2019 and 2021


*Dec 21

Figure from IQVIA digital health trends report 2021
When used as digital endpoints, there are differences between digital COAs and digital biomarkers

**Digital COA**
- COAs are defined as “a measure that directly describes or reflects how a patient feels, functions, or survives”
- When a COA is collected using a sensor technology, it’s called as digital COA

**Digital Biomarkers**
- Biomarkers are defined as “characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions”
- When a biomarker is measured using a digital tool, it’s called as digital biomarker

**Example: Gait Speed can be measured as a digital COA or digital biomarker**
- Gait speed can be used as a direct measure of how patient functions in their day to day
- **Example:** Gait speed when collected using Garmin foot pod was found to have a relationship with health related QOL in patients with ankle and foot pathologies
- Gait speed can be reflective of a pathogenic progress and has been shown to have a relationship with survival in older adults
- **Example:** Gait speed when collected using wrist worn accelerometer has been used as a susceptibility/risk behavior in men with HIV as an early indicator of declining mobility
In the context of Clinical Outcome Assessments, DHTs are a modality through which existing COA types can be advanced.

**Digital Health Tools (DHTs)**

- **Patient Reported Outcome (PRO)**
  - A measurement that comes directly from the patient

- **Performance Rated Outcome (PerfO)**
  - A measurement based on a standardized task(s) performed by a patient

- **Clinical Reported Outcome (ClinRO)**
  - An assessment determined by a trained medical professional

- **Observer Reported Outcome (ObsRO)**
  - An assessment determined by an observer (i.e., a non-clinician, such as a parent or caregiver)

* There is not consensus on continuous monitoring sensor data being classed as PerfOs due to the extent task standardization is achievable with them. Some opinion pieces simply classify as TechOs.
In clinical trials, evidence from DHTs can offer richer data and allow us to see beyond the data collected at clinic visits.

Traditional Data Sources...

...augmented with rich data streams from patient-generated health data.

6MWD at weekly check-ins

No. of steps taken per day
Digital medicine complements (but may not replace) traditional data sources to more fully understand the patient experience.

**Digital PRO data**

*Technology-Derived Data (DHTs)*

*active data collection via eCOA instruments*

*ePROs will tell us how patients feel about, and are impacted by, their physical functioning*

**Traditional PerfO data**

*Traditional COA data*

*active data collection via in-clinic PerfOs*

*In-clinic PerfOs will provide a measure of how actively the patient can perform on a test*

**Digital PerfO data**

*Technology-Derived Data (DHTs)*

*passive data collection via digital PerfOs*

*Digital PerfOs will provide a measure of how active the patient actually is day to day*
Regulatory guidelines on digital endpoints are recent, but demonstrate growing interest in the field

CTTI’s guidelines for developing novel endpoint generated by mobile technology

EMA’s Questions and answers: Qualification of digital technology-based methodologies to support approval of medicinal products

FDA Digital Health Center of Excellence

Pilot program for Innovative Science and Technology Approaches for New Drugs, including support to develop novel endpoints based on new technologies

DATAcc, a collaboration with multiple stakeholders such as the FDA and DiME Society to develop best practices and harmonized approaches

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations
Overall, the regulator and payer perspective on digitally collected patient generated health data are similar, but with some differences

- **Regulator**
  - Benefits/limitations of using digital technology vs. more traditional in-clinic assessment?
  - How to interpret meaningful change?

- **Payer**
  - Real-world benefits to collecting the data digitally?
  - What are the care pathway or patient outcome improvements?

Measures what it’s supposed to (e.g., *a step is actually a step…*)
- Collected systematically, reliably and accurately (validity)
- Clinically meaningful
- Patient relevant
- Correlates with a clinically relevant and *established* outcome
Sponsors need to demonstrate that the feature being captured has a direct link to patient relevant concepts and the disease

We have completed our review and decided not to accept your LOI. We have the following comments:

The Verily Study Watch/VME III measures a change in digitally assessed parameters of a subset of Parkinson’s disease motor signs from the MDS-UPDRS Part III (motor examination). However, the MDS-UPDRS Part III and the VME III are limited in their capacity to evaluate meaningful aspects of concepts of interest that are relevant to the patients’ ability to function in day-to-day life. For example, a change in rigidity or finger tapping in the MDS-UPDRS Part III cannot be directly interpreted as being meaningful to patients. However, a change in speech, eating and dressing (as assessed in the MDS-UPDRS Part II) represents meaningful change in how patients function in daily life. Additionally, the Verily Study Watch/VME III is a remote assessment that provides an algorithmic representation of change in selected items of the MDS-UPDRS Part III. This raises additional concerns about the ability to interpret changes on the VME III measured by the Verily Study Watch as representing meaningful change in patients’ ability to function. For example, it is unclear how the change in the digital signature for finger tapping (as measured by the Verily Study Watch) could be interpreted as representing meaningful change in patient function.

- FDA has rejected Verily’s request to use a wrist-worn wearable device to track changes in the motor symptoms of clinical trial subjects with Parkinson’s disease.
- FDA questioned whether the wearable device can show if an intervention has a meaningful effect on patients, leading it to reject Verily’s Letter of Intent.
When developing digital outcome measures, sensor features may be selected using a data-driven or a patient-centered approach to generate maximally sensitive or patient-relevant digital health technology outcome measures, respectively.

Data-driven digital endpoint:
- Model maximizes sensitivity
- Maximally sensitive sensor features

Patient-centric digital endpoint:
- Model maximizes patient relevance
- Patient-relevant sensor features

A digital outcome measure that uses a data-driven approach to summarize those sensor features maximally sensitive to the concept of interest.

A digital outcome measure that uses patient insights to summarize those sensor features that are optimally relevant to patients’ functioning in everyday life.
Although there is growing interest, there are three common pitfalls in the development of digital endpoints that are a barrier to regulatory approval:

**Pitfall 1: Lack of understanding of the patient-relevant concepts**
Example: “I saw a cool Apple watch at a conference, can we fit that in the trial somehow?”

**Pitfall 2: Starting too late & lack of planning**
Example: “At the beginning we just experimented, and now we need to go back and re-do some of the data collection”

**Pitfall 3: Lack of transparency in algorithms**
Example: “FDA/EMA requires clear demonstration of how the algorithm works, but the company won’t release details”

- Experimenting with new technology based solely on its appeal as something “new”
- Developing and testing digital measures without considering established frameworks such as design controls process
- Using proprietary algorithms from companies that do not disclose these to scrutiny of regulatory agencies
IQVIA has augmented guidance with literature and regulatory feedback to understand best practice for developing digital COAs.

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<thead>
<tr>
<th>Digital COA endpoints guidance principles</th>
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<tbody>
<tr>
<td><strong>Content Validity</strong></td>
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<td>• Find the meaningfu aspect of health (MAH) to measure with a device: the aspect of the patients’ health they want to improve or do not want to worsen</td>
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<tr>
<td><strong>Device/instrument identification</strong></td>
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<tr>
<td>• Identify which devices or instruments can measure concepts of interests derived from MAH using the sensors required</td>
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<td><strong>Analytic Validity</strong></td>
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<tr>
<td>• Assess if the DHT meets performance specifications (including accuracy, reliability, and validity) for the proposed intended use</td>
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<td><strong>Usability</strong></td>
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<td>• Understand how the patient interacts with the device in the real world or lab setting</td>
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<td><strong>Clinical/Construct Validity</strong></td>
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<tr>
<td>• Propose an endpoint using the DHT measurements and consider the statistical and measurement properties of this endpoint; assess the validity, reliability and responsiveness of the device</td>
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Justification of device selection and appropriateness for the context of use will have to be generated in accordance with principles similar to that of COA selection.
Key takeaways

Patient experience data is a topic of increasing interest

DHTs can be used to collect data to augment/supplement/enhance our understanding of patient experiences

DHTs are not new but regulatory focus and the novelty of concepts measured by DHTs in addition to increasing use as endpoints has led to widespread interest and adoption

Adoption is not a guarantee for success; there are a number of barriers and challenges to overcome

There is/are clear pathway(s), and when to the development of novel endpoint is done properly, we will start to see the opportunities being realized
Let’s continue the conversation

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