Digital Endpoints: Enhancing our understanding of the patient experience

June 2022

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Today's presenters

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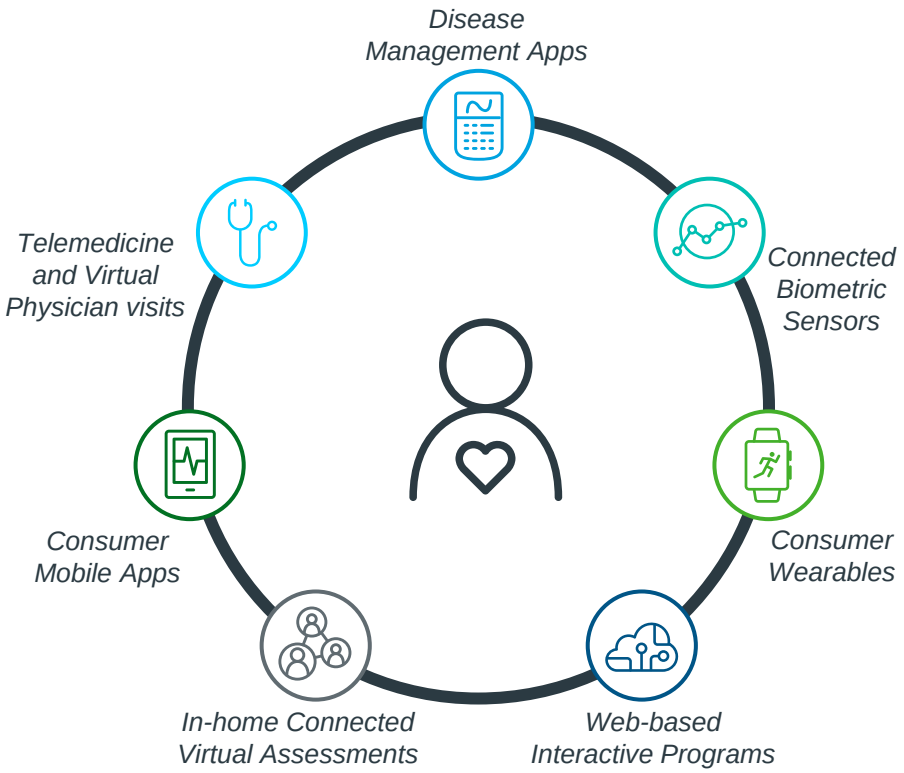
Today’s agenda

+ 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

Source: Figure from IQVIA MedTech

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"

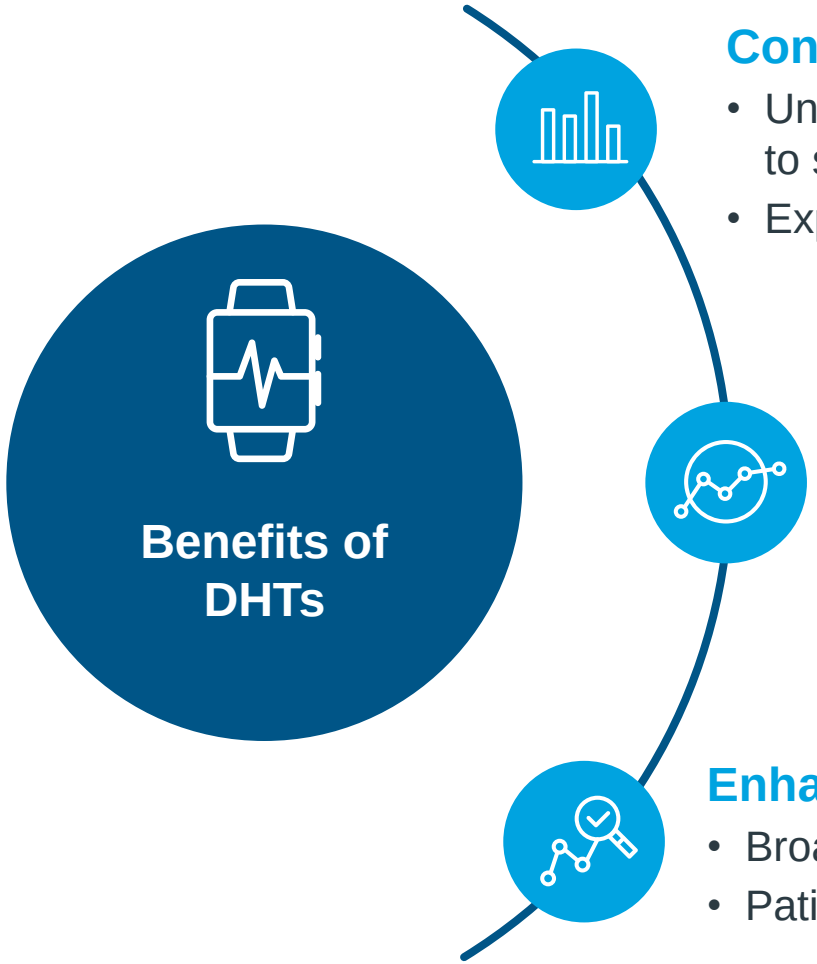
FDA provides a comprehensive definition of Patient Experience Data with acknowledgement of the importance of

- 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"**

Source: https://www.fda.gov/media/139088/download ; https://www.ema.europa.eu/en/documents/presentation/presentation-ema-regulatory-science-2025-reinforce-patient-relevance-evidence-generation_en.pdf
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

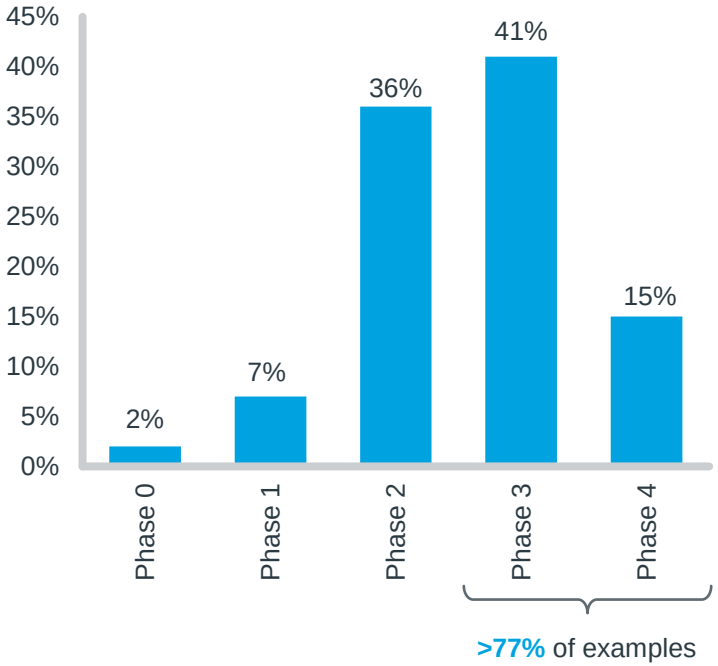
Enhanced understanding of patient experience

- 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

Sponsors start digital endpoint development early

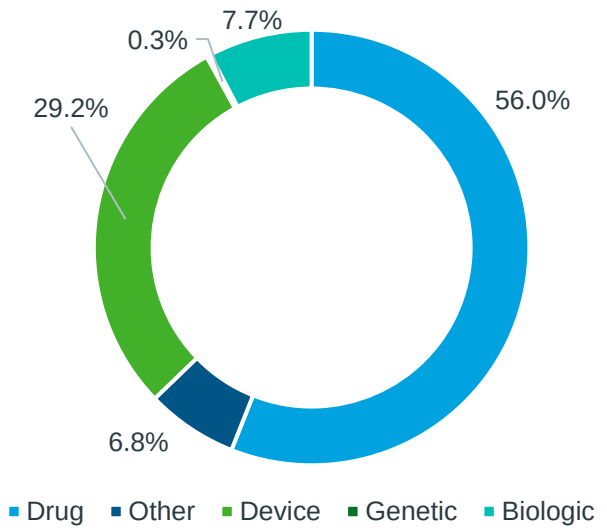
Digital Endpoints



>77% of examples

Digital endpoints are being used across drug, device, biologic, and genetic product development

Investigational Product



Pharma trusts digital products, primary/ secondary endpoints

Endpoint Positioning

98	Primary endpoints
182	Secondary endpoints
19	Other
6	Exploratory
305	**Unique Endpoints**

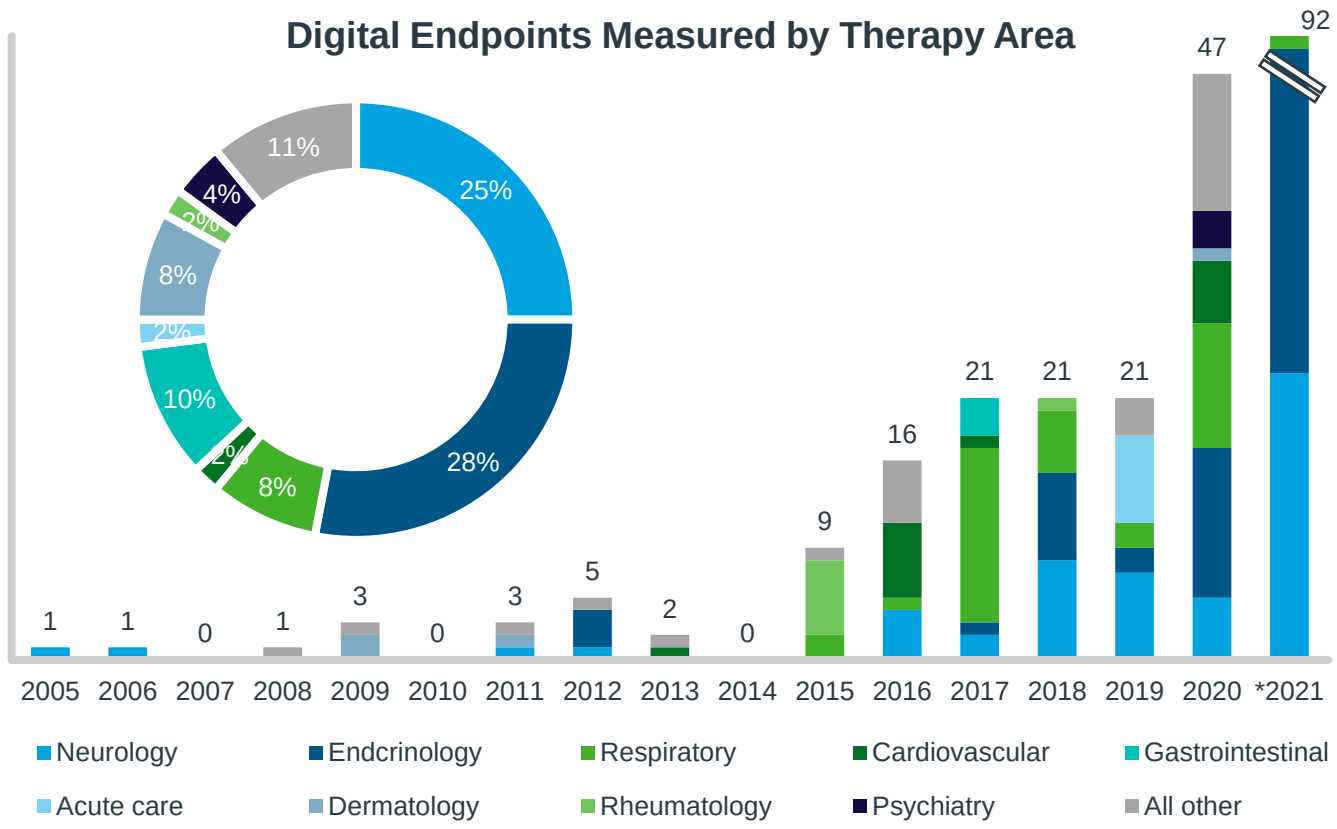
**Only drug trials with reported phases are included*

"Source: Digital Medicine Society (DiMe) Library of Digital Endpoints https://www.dimesociety.org/communication-education/library-of-digital-endpoints/"

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

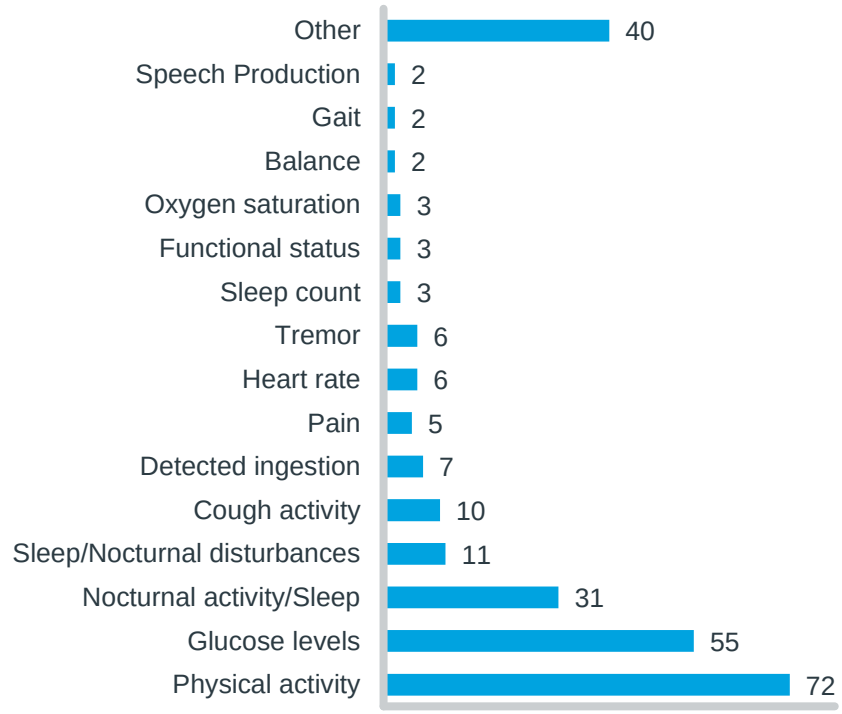
N = 118 Distinct Trials with 244 Distinct Digital Endpoints

Digital Endpoints Measured by Therapy Area



Health Concepts Tracked by Digital Endpoints

N = 258



"SOURCE: Digital Medicine Society (DiMe) Library of Digital Endpoints https://www.dimesociety.org/communication-education/library-of-digital-endpoints/" *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*

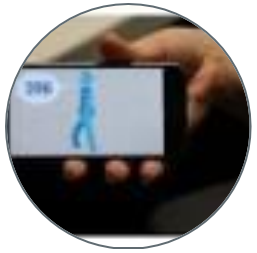
BEST Glossary; FAST Facts: Digital Medicine - Measurements

In the context of Clinical Outcome Assessments, DHTs are a modality through which existing COA types can be advanced

Digital Health Tools (DHTs)

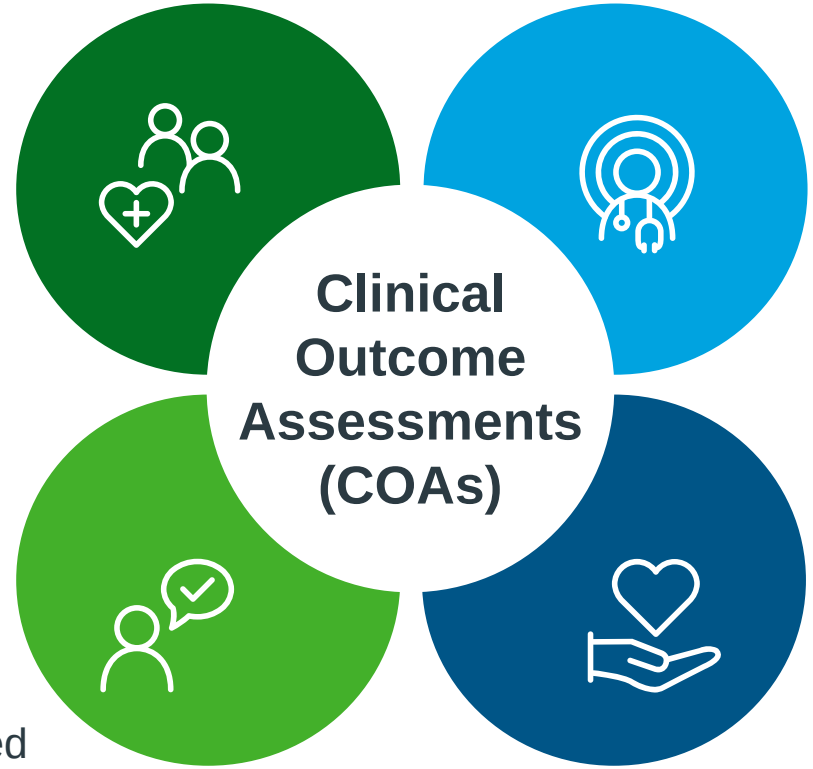
Patient Reported Outcome (PRO)

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***

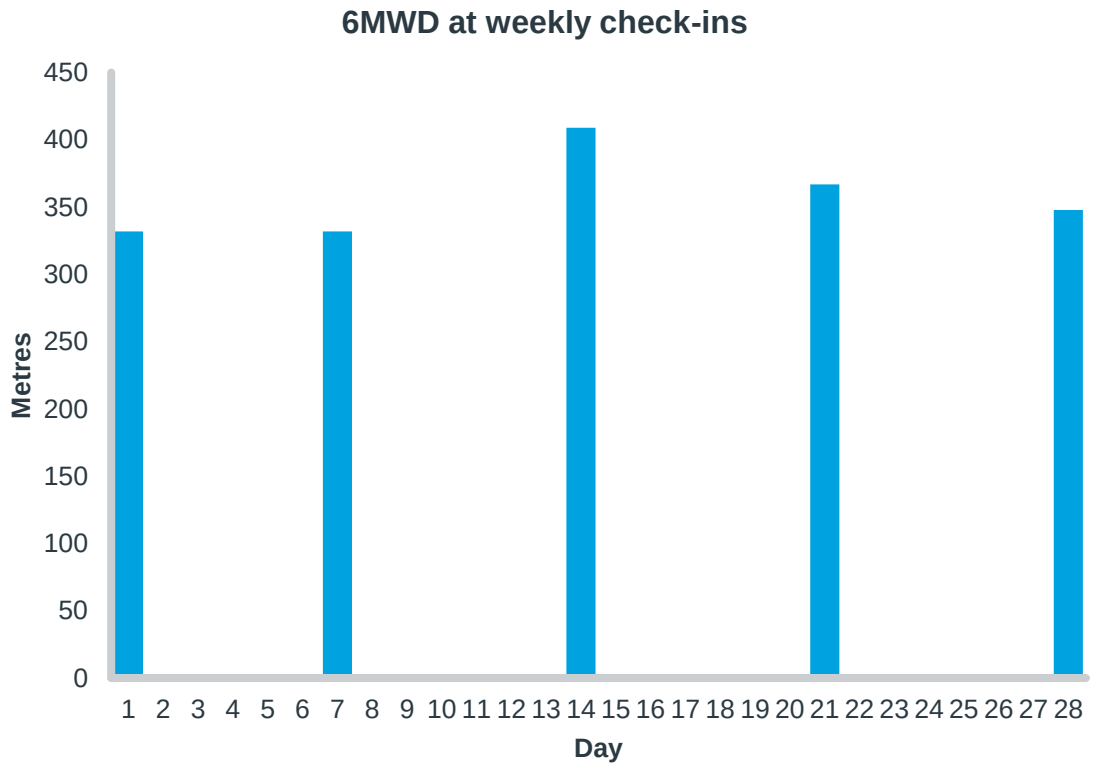
Observer Reported Outcome (ObsRO)

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

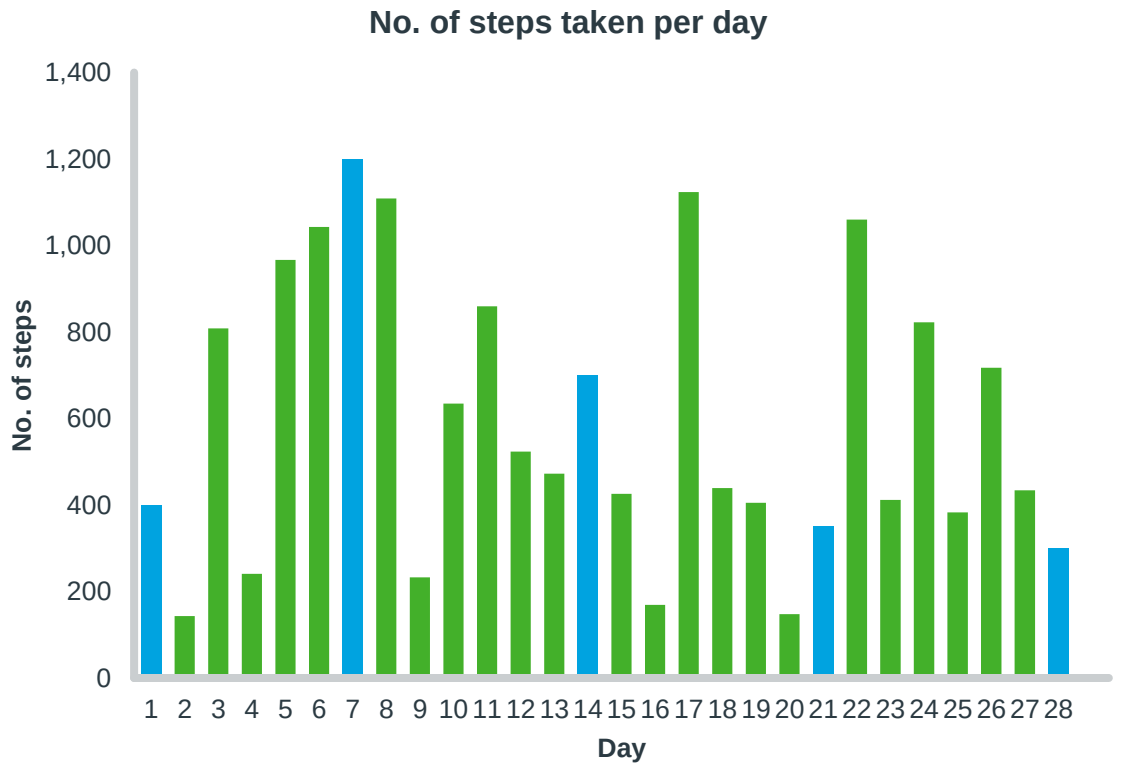
* There is not consensus on **continuous monitoring sensor** data being classed as PerfOs due to the extent task standardization is achievable with them. Some opinion pieces simply classify as TechOs

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



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

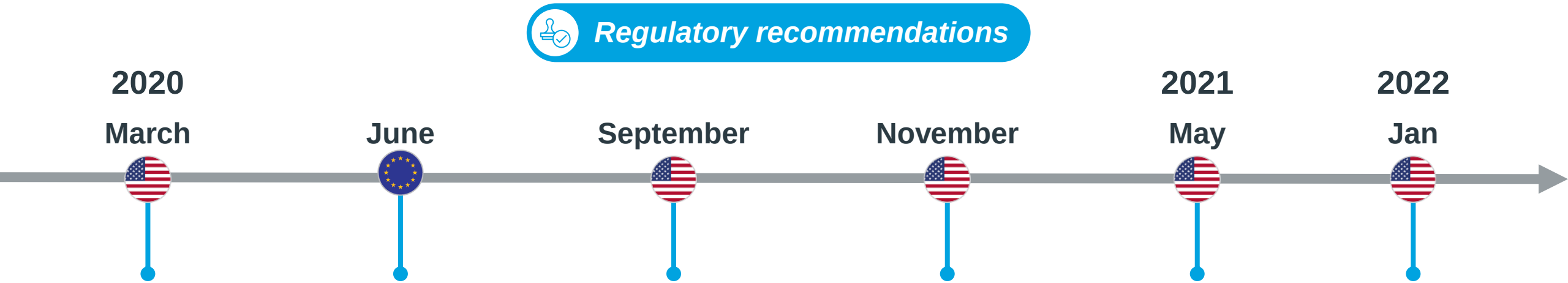
Digital PerfO data

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?

Sponsors need to demonstrate that the feature being captured has a direct link to patient relevant concepts and the disease

FDA U.S. FOOD & DRUG ADMINISTRATION

DRUG DEVELOPMENT TOOL
LETTER OF INTENT DETERMINATION
DDT COA #000142

Dinesh Puppala, MS
Verily Life Sciences

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

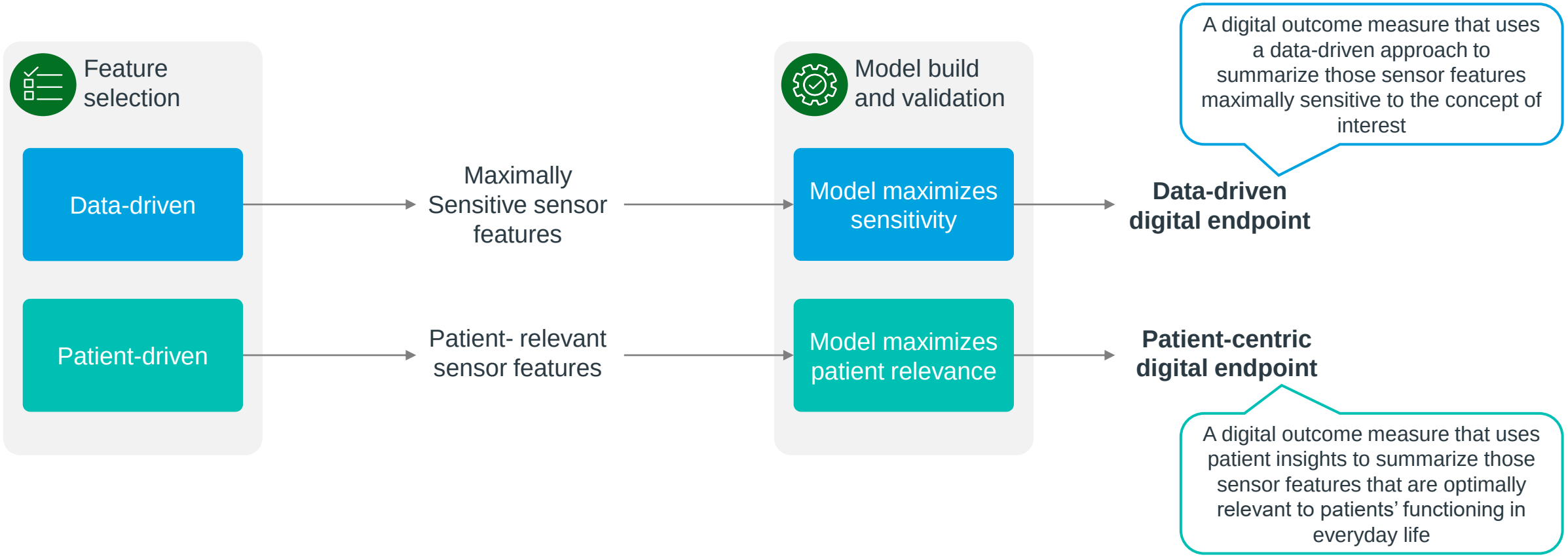
The Verily Study Watch/VME III measures a change in digitally assessed parameters of a subset of Parkinson's disease motor signs from the MDS-UPDRS Part III (motor examination). However, the MDS-UPDRS Part III and the VME III are limited in their capacity to evaluate meaningful aspects of concepts of 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

MDS-UPDRS: Movement Disorders Society Unified Parkinson's Disease Rating Scale

Digital endpoints can be developed using a patient centric or a data driven approach

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



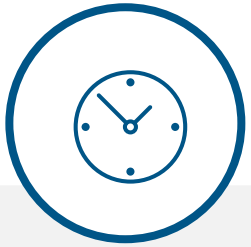
Taylor et al. Outcome measures based on digital health technology sensor data: data- and patient-centric approaches

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?”

Experimenting with **new technology based solely on its appeal as something “new”**



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”

Developing and testing digital measures without considering established frameworks such as design controls process

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”

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

Digital COA endpoints guidance principles

Content Validity

- Find the **meaningful 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

Device/instrument identification

- Identify which devices or instruments can measure concepts of interests derived from MAH using the sensors required

Analytic Validity

- Assess if the DHT **meets performance specifications** (including accuracy, reliability, and validity) for the proposed intended use

Usability

- Understand how the patient interacts with the device in the real world or lab setting

Clinical/ Construct Validity

- **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

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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