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WHITE PAPER

Developing Your Mobile Sensor Strategy Journey for Better Study Outcomes

Defining a Focused Data Strategy is Key

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Introduction

Several key factors have accelerated the uptake of digital health technologies (DHTs) in clinical trials, including an increased market demand in general for digital technologies, the COVID-19 pandemic, and increased acceptance of DHTs by regulators.

Despite a well-documented array of benefits of DHTs in clinical trials, the life science industry must overcome some important challenges to fully unleash their potential. Given the aggressive growth of DHTs (which can include any connected health device) in clinical trials, coupled with an increasingly large selection of possible devices, this white paper highlights key factors that should be taken into consideration as Sponsors and CROs develop their DHT strategy.

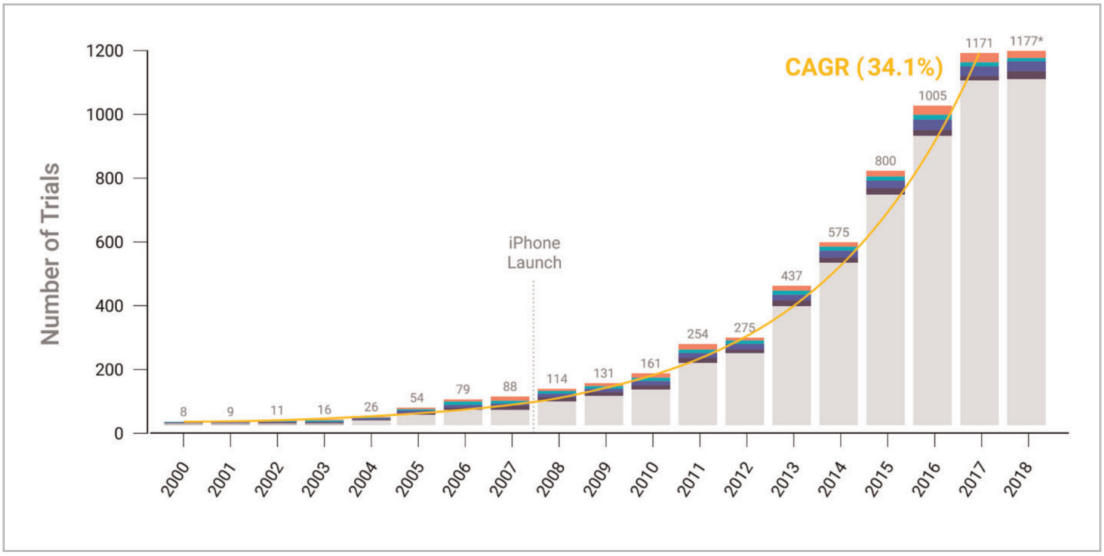
Planning your data strategy prior to starting a trial will maximize the opportunity that your DHT will provide high quality and compliant data that can effectively withstand regulatory scrutiny. Robust planning allows clinical trial teams to mitigate risks, such as ensuring that optimal devices are selected based on specific study and patient needs, and that the devices can be seamlessly integrated into the workflow.

The Rising Adoption of Digital Health Technologies in Clinical Trials

Major advances in wireless technologies and computing power have been driving outstanding innovations in medical devices, and with an estimated 6,500 medical device companies in the U.S. (ReportLinker, 2020), it comes as no surprise that there is a rapidly growing market for DHTs in clinical trials that can generate, collect, and transmit high-frequency, high-volume data (Deloitte 2018).

As shown in Figure 1, a significant shift in growth began in the year 2000, with a compound annual growth rate of greater than 34% for the number of trials using DHTs, which are being employed across all phases of clinical development (Marra, 2020). Further, a recent analysis suggests that while approximately 10–15% of trials are currently using DHTs, this number is expected to significantly increase, to 70% in the next 5 years (Myshko, 2019).

Figure 1: Clinical trials using connected digital products by study start year and phase. From Marra et al. (2020). Quantifying the use of connected digital products in clinical research. npj Digit. Med. 3, 50 (2020). https://doi.org/10.1038/s41746-020-0259-x. Used under Creative Commons Attribution 4.0 International license: https://creativecommons.org/licenses/by/4.0/



At the same time, there has been an increased focus on creating more patient-centric clinical trials. This trend has been fostered by regulators' increased backing of digital tools for clinical trials to collect more objective measures, such as the U.S. Food and Drug Administration's (FDA) Digital Health Innovation Action Plan, launched in 2017 with the goal of accelerating digital health advancements (FDA, 2017). Further, in their draft guidance on heart failure, the FDA explicitly discussed the use of accelerometry as a novel endpoint that will be considered as a measure of heart failure and to assess effects of treatment (FDA, 2019).

More recently, due to the COVID-19 pandemic, the FDA and European Medicines Agency both issued guidance documents describing important changes, such as use of remote site and patient monitoring technology, to allow clinical trials to continue safely (FDA, 2020; EMA, 2020). According to one study, the pandemic led to approximately 6,000 clinical trials being halted between January and May 2020 (Gaudino, 2020). Consequently, industry had to rapidly adapt ongoing and new clinical trials to incorporate more virtual elements, such as remote monitoring, as these approaches "may serve to give sponsors and regulators confidence that they can be effectively deployed in non-emergency conditions" (Hinkle, 2020).

Despite a dizzying array of possible DHTs, Sponsors and CROs should consider their trial objectives prior to selecting their DHTs. For instance, if they intend to use them to develop algorithms and analytics that will be part of a regulatory submission, then medical-grade DHTs would be most appropriate. This underlying point is the crucial distinction between the consumer-oriented devices and the more sophisticated medical-grade sensors. As compared to most consumer-oriented DHTs, medical-grade DHTs are required to undergo a more rigorous evaluation process because they must adhere to stringent regulations and requirements, since medical professionals may use them to make a diagnosis or guide clinical decisions. Prior to selecting a device, you should consider its accuracy, reliability, privacy, and security and which metrics have been validated for that specific device. Further, to ensure your trial is patient centric, you should also consider ease of use, form factor, and the availability of a companion application.

Together, DHTs are increasingly providing data streams that were previously not possible, such as real-world evidence collected from patients in their natural environment. This wealth of data has sparked exciting opportunities for developing novel digital biomarkers and endpoints to facilitate groundbreaking insights.

However, many potential bumps in the road must be considered prior to implementing DHTs in clinical trials. With the appropriate up-front planning, common pitfalls can be identified and circumvented so that the DHT strategy is appropriately structured before starting the trial. This not only maximizes the chances of a successful trial but also enhances the likelihood that regulators will accept the submitted data and conclusions.

Industry Challenges

Deploying DHTs in clinical studies is not a one-size-fits-all approach. Sponsors and CROs face many challenges, which, if not managed appropriately, can result in poor trial performance and patient outcomes, which can lead to drug development delays.

From a sensor and data strategy perspective, the major industry challenges fall into three related areas:

- ✓ Technical challenges are often encountered when integrating disparate data sources, due to the lack of common standards, which can frequently lead to interoperability issues. Another important technical challenge that must be addressed is the security and privacy of the trial data for not only the immediate studies at hand but also compliance for future regulatory submissions, which may require merging different datasets. Patient comfort level with technology is another key challenge that must be tackled to ensure patients will accept and use the DHT as intended throughout the entire length of the trial.

- ✓ Logistical challenges largely revolve around selecting the best-fit DHT(s). As noted earlier, medical-grade DHTs are typically preferred, and with so many options to choose from, you want to make sure to select the optimal DHT for your specific trial, to ensure the greatest chance of success and that it can be efficiently integrated so that cost, time, and effort of integration are within scope. You must also consider how the DHT will be managed and supported and whether there may be regulatory differences across geographic regions that might impact deployment in a specific region.

- ✓ Analytical challenges can quickly overwhelm an unprepared infrastructure. High-velocity medical-grade and clinical DHTs can generate massive streams of data that often need to be visualized and analyzed on an ad hoc basis. Another layer of complexity occurs when disparate DHTs are connected, since they often have different output measures and they format those measures differently.

To overcome these challenges, scalable and secure software solutions are required to manage the high-volume, high-velocity data that will have to move through a workflow that seamlessly enables analytics and visualizations that can be used to facilitate novel insights. Having an effective plan to deal with the challenges can position your trial for success and, as a result, maximize the likelihood that regulators will support the conclusions from your submitted data. A common data model is one way to address these challenges.

A Common Data Model

Leveraging a common data model built on well-established clinical vocabularies and technical standards (such as the Sensor Open Systems Architecture [SOSA], Unified Code for Units of Measure [UCUM], Fast Healthcare Interoperability Resources [FHIR], Logical Observation Identifiers Names and Codes [LOINC®], SNOMED CT), can facilitate analyses across disparate data structures, including other non-sensor data streams. Importantly, using a common data model allows drug developers to stay focused on the implications of their analyses rather than expending time and resources on the nuances of ingesting and harmonizing disparate datasets.

> Using a common data model allows drug developers to stay focused on the implications of their analyses, rather than expending critical time and resources on the nuances of ingesting and harmonizing disparate datasets.

A common data model can merge datasets from current and past studies with different DHTs. Despite differences in outputs (based on similar metrics), when data are processed through a common model, they are standardized in a way that allows for like-to-like comparisons, and these new data sets contain information that is being used to achieve the following:

- ✓ Generate insights for the discovery of new digital endpoints and biomarkers for monitoring patients to assess safety and efficacy of a treatment or intervention or disease progression, for instance. These insights can also support commercial endeavors, such as pursuing label extensions and value demonstration and reimbursement.
- ✓ Enable machine learning techniques, which are notoriously difficult to apply to disparate data. A common data model allows for development of algorithms across multiple datasets that have been collected in different clinical settings but are organized with similar annotations so that data patterns can be observed quicker.

Implementing an Integrated Data Strategy

As the clinical trials industry continues to evolve and mature, data will increasingly become standardized, and comprehensive data strategies will be proactively established to enable the development of novel endpoints, in contrast to the retrospective method that is typical now.

INTEROPERABILITY IS KEY

As an increasing body of clinical data streams becomes available (e.g., lab test results, imaging data, safety data, eCOA, eConsent, DHTs), an interoperable platform can serve as the hub that connects the disparate parts of the ecosystem so they can communicate with each other and ensure that the different data streams are gathered in a way that allows for data analysis.

Selecting an optimal collection of DHTs, coupled with an interoperable platform, serves as the foundation for establishing a decentralized clinical trial platform, which has the advantage of enhancing patient-centricity—which entails many benefits, including improved patient recruitment and retention—and enabling the collection of more personalized data that is continuous and objective.

CLINICAL DATA AS THE ANCHOR

Depending on the nature of the endpoint data, if the goal is to develop a new endpoint, it is important that the DHT data capture is directly linked and compared to clinical data. This approach provides the best opportunity for obtaining specific claims from regulatory bodies based on DHT data. The right interoperable platform, DHTs, and data strategy need to be optimal to facilitate this process. It is simply not enough to select a great DHT and operational partner. Without a robust clinical anchor, data analyses based on the DHT alone are meaningless and less credible arguments can be made, which can increase the risk of failing to reach your study objectives.

> "Regarding regulatory challenges, Hawkins said she has found regulatory agencies to be quite interested in working collaboratively to implement and pilot these new digital technologies in the context of clinical trials. An important concern, however, is endpoint validation using a specific digital health technology, which requires implementing a time to validate the technology into a clinical development plan."
>
> Kimberly Hawkins, Clinical Sciences and Operations Project Leader Head at Sanofi Genzyme (as quoted in Shore, 2019).

ENRICHMENT OF SUBJECTIVE DATA

Clinical endpoints are developed, and drugs are approved by regulators, based upon patient outcomes, survival, and quality of life (QOL), and activity of daily living (ADL).

DHTs can be integrated with and enhance subjective measurements (e.g., eCOA and ePRO) that are collected to evaluate how patients feel and provide highly contextual functional assessments based on objective data. Monitoring both the subjective and objective measures can develop a more complete patient picture to support approval of specific claims, for instance.

BENEFITS ARE WIDE RANGING

The benefits of an integrated data strategy are wide ranging and include the following:

- Facilitate the development of novel endpoints.
- Measure performance in the post-approval setting, which may be used to pursue label extensions.
- Enhance safety monitoring capabilities, which can allow for detecting signals earlier, either during clinical development or in the post-approval stage.
- Continuously measure data from medical-grade DHTs, which can potentially and favorably alter the statistics associated with clinical trials. This is because signals may be detectable with fewer patients which can change the cost structure of larger trials, since more data points may reduce the required trial size.
- Potentially reduce costs through higher patient retention, fewer site visits, and faster overall trials.
- Enhance recruitment; since DHTs and decentralized trials bring clinical trials to patients, they can lower the patient burden and widen the possible patient pool. Older patients want to engage with new technologies as reported by Baca-Motes et al. (2019) who showed that recruitment efforts for attracting patients aged 55+ into a clinical trial were maximized when the focus was that they would be engaging with a new technology.
- Applicability that cuts across multiple therapeutic areas, including, but not limited to oncology and Parkinson's disease (PD). In the instance of oncology, it is well documented that changes in heart rate, sleep efficiency, and actigraphy are all associated with survival. Thus, by using DHTs to measure heart rate variability and sleep efficiency over time, abnormalities can be detected earlier, and interventions applied sooner, which may enhance survival. For PD, the following section describes two studies that successfully used DHTs in this patient population.

Two Sensor Studies in Parkinson's Disease Patients

The clinical assessment of PD motor symptoms has traditionally been done in a subjective manner and the degree to which this reflects the patient's real-world experience is not entirely known. Using DHT approaches, two studies sought to expand our understanding of PD motor symptoms using a patient real-world experience perspective. Together, these studies highlight the value of DHTs for:

1. Moving clinical assessments to the home which reduces patient burden and improves accuracy, and
2. Developing new endpoints in patient populations that are geographically dispersed.

The first study by Boroojerdi et al. (2019) was a collaborative effort between UCB Pharma and MC10, Inc. [acquired by Medidata in 2020]. This was a two-part pilot study which was conducted to assess the accuracy of the "NIMBLE" wearable biosensor patch containing an accelerometer and electromyography sensor. PD patients on a stable levodopa dose with motor symptom fluctuations were enrolled. The sensor versus clinical measurements of motor symptoms were compared by recording body movements in the clinic and the home environment.

The first part of the trial looked at different body locations for optimal placement of the sensors, while the second part assessed motor symptoms after placing four sensors on patients during a 2-day clinic and 1-day home evaluation that was based on the Unified Parkinson's Disease Rating Scale. Overall, the authors reported that the correlation coefficient between in-clinic observed and sensor algorithm-predicted scores was 0.471 (p=0.031), and the predicted and observed scores were identical 45% of the time and the exact accuracy for each activity varied, ranging from 32% (pronation/supination) to 67% (rest-tremor-amplitude). According to the investigators, this study showed a correlation between sensor algorithm-predicted and clinician-observed motor symptom scores and refinements may further improve this correlation (Boroojerdi 2019).

In a second study, researchers at the University of Rochester in collaboration with MC10 Inc. sought to determine the feasibility of using wearable sensors (BioStampRC®) to determine the activity (lying, sitting, standing, walking) of PD patients (and Huntington disease patients). Subjects had accelerometer-based sensors placed on their chest and limbs for standardized in-clinic assessments and for two days at home. Overall, the authors found that the sensors identified statistically significant differences in activity profiles between individuals with movement disorders and those without. The authors indicated that "continuous, objective monitoring can reveal disease characteristics not observed in clinic" (Adams, 2017).

Summary

DHTs have experienced a significant uptake in clinical trials over recent years, and this trend is expected to rapidly increase into the foreseeable future. However, as discussed in this paper, DHTs are not necessarily a panacea. There are many challenges that companies face when embarking on a trial with DHTs, and without an adequate data strategy in place, trials face an increased risk of failure from both an operational and regulatory perspective.

To fully exploit the benefits of DHTs and improve the odds of trial success, companies need to engage in upfront strategic planning to ensure they are considering the optimal DHTs for their specific trial needs, that the DHTs will fit into their clinical workflow, and that the data will be captured in a compliant manner that can be analyzed and visualized efficiently.

DHTs are unlocking many powerful insights that were not previously possible, and as their adoption continues to rise, companies need to be aware of the potential pitfalls in order to maximize success for patients, sites, CRO's and sponsors.

MEDIDATA SENSOR CLOUD

Medidata Sensor Cloud provides cutting-edge capabilities focused on transforming the clinical trial experience for patients, sponsors, and research sites. Designed as part of a unified data platform, Sensor Cloud takes a unique approach to managing a broad range of wearable sensor and digital health technology data for clinical trials. Our common data model and proprietary algorithms enable rapid ingestion and analysis of patient data resulting in better clinical decision making, faster timelines and a more flexible patient experience.

To learn more about the Medidata Sensor Cloud, get in touch by visiting
https://www.medidata.com/en/medidata-sensor-cloud

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