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Transforming Clinical Trials: The Path To A Successful Digital Trial

Thought Leadership In Association With ICON

by

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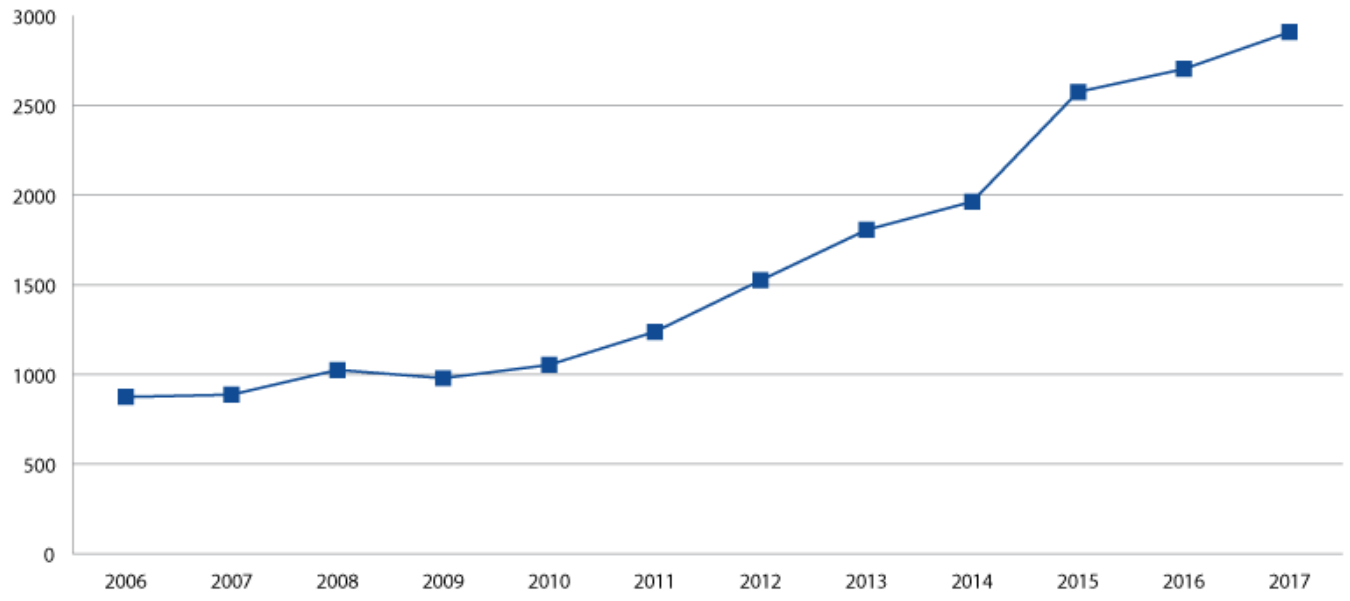
Authors:

Marie Mc Carthy, Senior Director Product Innovation, ICON

Chen Admati, Head of Intel® Pharma Analytics Platform, Intel

Over the last number of years the use of mHealth technologies has been increasingly embraced by patients, healthcare providers and payers. Connected health ecosystems have been evolving at a rapid pace and it is now believed that the IoHT (Internet of Healthcare Things) market will be worth $163 billion by 2020[1]. It has been estimated that over 7.1M patients worldwide benefit from remote monitoring and the use of connected medical devices as part of their care regimen[2], to better inform and educate themselves about their disease and to share their knowledge with each other. This patient empowerment is reflected by the estimate that 1 in 20 Google searches is healthcare related[3]. mHealth device technology has evolved to the point where it is now possible to collect a vast array of physiological data including vital-signs such as heart rate, respiration rate, oxygen saturation, continuous glucose monitoring, sleep and activity data, and

using advanced analytics to monitor patients in their own home outside the hospital environment. There is a growing awareness in the healthcare sector of the benefit and value of a mHealth approach to healthcare. As early as 2013 as a way of maximising healthcare spending, sleep apnoea patients in France have been monitored remotely to ensure they are compliant in the use of their CPAP (continuous positive airway pressure) devices.This has led to new care models in mobile health, for example, University of California, Los Angeles actively promote their remote patient monitoring program as having positive values for patients and their primary healthcare teams to manage their health "from the comfort of your own home" and to reduce hospital admissions and emergency room visits[4]. However the penetration and use of wearables and devices in the pharmaceutical industry is still limited. But interest in mHealth/digital technology is apparent with nearly 3000 articles published in peer reviewed journals in 2017 (PubMed), an almost 100% increase on the number published five years earlier.



The value of the technology is clear—in a recent industry survey for the ICON whitepaper 'Improving Pharma R&D Efficiency' respondents cited big data, predictive analytics, smartphones and wearables & sensors as amongst the top disruptive technology trends which will have the greatest impact on clinical trial operations.

So the question remains, in the context of drug development studies, why has the use of this technology been limited to a relatively small number of pilots? It is clear that concerns still remain about implementation of this technology in a clinical trial. These concerns focus on a number of key areas: Patient Acceptance, Device Suitability, Data Complexity and Insight Generation, Operationalisation, Privacy and Security Issues, and Regulatory Acceptance.

How To Implement Successful Digital Clinical Trials

#Patient Acceptance. Patient recruitment and retention are key issues for clinical trials. While it is generally accepted that the use of devices and sensors can help create more patient centric studies, if not carefully managed digital technology can add additional burden for the patient. This is a critical factor when integrating devices and sensors into a study; ensuring your study design has a 'maximum passiveness' approach is key. Data collection should be as seamless as possible with minimal actions required from the patient. Selection of a low-burden device that is simple to use with an attractive form-factor is another important aspect for increasing patient engagement. The device should, where possible, support both iOS and Android operating systems to allow for a BYOD (bring your own device) model. A single study app, that acts as the interface between the individual and the trial and includes features to support the patient in his/her day-to-day life, must also reflect the disease specific characteristics. These apps need to be designed with the user experience in mind and should add value to the patient experience while part of the study. Lastly, compliance monitoring has proven to be a significant contributor to the success of digital trials. Proactively flagging non-compliance and utilising a multi-faceted approach to engage with patients; from app to SMS notifications to direct contacts contacting patients, can help drive greater compliance and ensure optimal data generation and capture.

Device Selection. New devices are launched almost every day and selecting the right device is a challenging task and poses a number of critical questions; so how to choose? Should we use single or multiple devices? Medical grade devices or consumer technology? Unfortunately there are no simple answers, and certainly there is no one device that can be used in all studies. There are some publications that provide guidelines[5] and can support the selection process. Of primary importance is the selection of a device that can generate the data required to meet the study needs. The device itself must be fit for purpose: have high usability such as long battery life, be form factor appropriate for the study population, and facilitate the collection and transfer of the required data. The trial design will guide the device(s) selection process, if a device is being selected to support an endpoint, ensuring there is sufficient scientific evidence to support the use of that device is critical. If a device is being used to track trending and changes, or is used in late phase studies, greater choice exists in terms of the devices being selected for use.

Data Complexity and Insight Generation. Existing clinical studies rely to a large extent on results from monthly outcome assessments carried out in a clinic. The potential to generate new insights from continuous measures captured as patients go about their lives is significant. If we take as an example a typical Phase II clinical trial in CNS: a few dozen patients, participating in a trial for a few months to a year. Let's assume we would like to capture objective insights and provide these patients with a wrist-worn device equipped with a 50Hz accelerometer and gyroscope sensors. The use of such a device will generate nearly 1 billion data points per day. Combining these data with ePRO (electronic patient-reported outcomes) methods, along with and other physiological data such as heart and respiration rates can create a big, complex dataset that is beyond the capacity of standard electronic data capture (EDC). Therefore, when

selecting a digital platform, the ability to scale and ingest high frequency datasets is important. In order to generate insights and digital biomarkers, skilled experts in advanced analytics, data scientists, are needed. The platform should enable the data scientists' work by exposing the appropriate tools to process the data and run machine learning algorithms.

Operationalisation. The art of simplicity is a puzzle of complexity. When running a successful digital trial, there are multiple stakeholders and processes involved. Device selection, device purchasing, application setup, device distribution and reconciliation after the study, IRB submission, patient and site training, and patient support are some of the challenges facing the study team. Establishing and structuring data sourced from diverse systems can also be technically daunting. An experienced study team with a strong patient engagement element and a reliable, robust digital framework is required to ensure delivery of an end-to-end solution out-of-the-box with full integration.

Privacy and Security. With increasing concerns on data privacy and security, these issues must impact the selection of the digital platforms as well as the trial design. A chosen platform must meet industry standards such as HIPPA, GDPR, and ISO 270001. Decisions on where to locate the trial globally may introduce new data privacy requirements. When collecting and storing the data, all data needs to be pseudonymised in accordance with local regulations. Patients need to be appropriately consented, particularly with regards to the use of the data. This will become even more significant as the value of the collected data lies not only in the study for which it has been collected, but also in its potential value for meta-analysis and the testing of new and yet unidentified algorithms.

Regulatory Acceptance. As with all trials, the recommendation is that early engagement with the regulators is required. There are a number of roadmaps and recommendations from both the Clinical Trials Transformation Initiative (CTTI)[6] and the ePRO Consortium[7] that can be used as reference when considering the integration of digital technologies in trial design. Regulators are also striving to support the use of digital technologies in clinical trials. The US Food and Drug Administration in particular, is actively participating with stakeholders to be in a position to offer guidance on the use of digital and mHealth technology and have recently launched a digital technology website[8] and a Digital Health Innovation Action Plan[9].

Summary

Declining research and development (R&D) efficiency is one of the biggest challenges the pharmaceutical industry is facing today. The traditional approach of three discrete, fixed trial phases designed for testing mass-market drugs often is not viable in today's increasingly competitive, value-based therapeutic markets. It lacks the flexibility, analytic power and speed required to develop complex new therapies targeting smaller and often heterogeneous patient populations. As a consequence, clinical trials are changing. Digital disruption in the form of new wearables, sensors and medical devices enable pharmaceutical and medical device companies to

generate new types of datasets. Artificial intelligence and machine learning can generate new insights and digital biomarkers that have the potential to be more clinically responsive to change. However, to run a successful remote/digital trial, a complete end-to-end solution is required. Carefully selected technology, combined with the right trial design and operational excellence, will increase the likelihood for success.

www.iconplc.com/digital

www.intel.com/healthcare

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About ICON

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