Wearable Technology: Transforming Clinical Research?

Use of wearable technology in clinical studies has the potential to drive dramatic changes in clinical research practices, to reduce the cost of clinical trials, and to maximise their impact.

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Introduction

The last 10 years have seen a dramatic increase in the use of wearable devices, largely driven by the burgeoning interest in health and fitness. The majority of these wearable devices, Fitbit, Jawbone, Moov, and others, are relatively cheap and are firmly targeted at the consumer market. The rising prevalence of lifestyle diseases such as obesity has led to an interest in the use of such devices to monitor and alleviate these conditions, and also to a growing realisation of their potential value in monitoring patients in related clinical studies.

Wearable devices can now readily measure health-related functions such as step count, sleep quality, gait, heart rate, blood pressure and temperature, while the more sophisticated devices can also measure respiration, oxygen saturation, ECG, glucose levels and galvanic skin response[1]. The integration of wearable health monitors with smartphones offers further capabilities, either to transmit health measurements directly to caregivers through wireless technology, to monitor drug adherence, or perhaps most significantly, to collect continuous and accurate health data in real time. Widespread use of such wearable devices in clinical studies has the potential to transform and revolutionise drug development by the pharmaceutical industry.

Application to clinical studies

A number of medical devices such as spirometers[2] and activity monitors[3] have been adapted over the past decade for use in clinical trials. However many wearable devices are now being specifically designed with a primary function of medical monitoring in mind. The main feature of these devices is the incorporation of embedded technology, which can facilitate the secure collection and transfer of large amounts of data wirelessly. This allows health data from the subject to be collected effortlessly in the background, in the 'real world', lowering the impact on both patient and study centres, and increasing the validity of the data.

The therapeutic areas where healthcare organisations are starting to implement use of wearable devices are the most prevalent chronic illnesses: diabetes, hypertension, congestive heart failure (CHF), and chronic obstructive pulmonary disease (COPD). However it is clear that wearables can also make a significant impact in therapeutic areas where outcomes are linked to quality of life measurements that can be assessed through improved vital signs and movement. One area that is likely to see a rapid expansion of the use of wearable devices is in neurological conditions, such as Parkinson's Disease[4] and Alzheimer's Disease.

In addition, wearables can positively impact studies where a patient record or diary is required, particularly through improving compliance using prompts and reminders, and by simplifying the record-taking process. Finally, ingestible monitors that can collect data on medication consumption, dose scheduling and physiologic responses, then transmit measurements to a recording device such as the patient's smartphone, are becoming more widely available[5].

Potential impact in clinical studies

Pharmaceutical companies are determined to increase the efficiency and efficacy of their drug development processes, and to thoroughly understand and differentiate the drugs in

their development pipeline. Late stage clinical studies represent one of the major costs of the drug development process, and hence hold great potential for cost savings. There is a huge appetite for technological solutions that can assist companies in their quest for improved drug development practices, including the use of wearable technology in clinical studies.

The potential benefits of wearable devices include:

- Real-world, continuous and passive measurement of a patient's health through unobtrusive tracking of vital health measurements and related data during their daily routines, with the prospect of developing richer and more complex patient health profiles.
- Reduced overall costs for clinical studies through a decrease in the number of expensive in-clinic patient visits, as patient data can be transferred directly and continuously to the research site.
- Increased participation in clinical studies from a wider population of patients who may not live near a study centre.
- Decreased variability of data and increased consistency through collection of larger amounts of data, allowing fewer patients to be recruited into the study in order to achieve the required statistical significance.
- Enhanced data collection to improve the accuracy of patient-reported outcomes (PRO), and to better understand the nature of any adverse events (AE).
- Improved patient compliance and retention through the delivery of suitable prompts, and hence with more convenience, to encourage study participation.
- Perhaps more speculatively, developments in predictive analytics offer the potential ability to alert researchers to future AEs before they occur, based on data analysed from both individuals and populations.

Clinicians have not previously been able to derive information about lifestyle changes between visits to the doctor's office or research centre, unless self-reported by the subject, which is

potentially subject to bias. The continuous collection of health-related data from wearables can provide valuable insights into relevant details of a patient's well-being, such as association of activity levels or transient spikes in blood pressure with drug ingestion and dosing. The researcher can then be alerted to any specific effects on the patient's lifestyle and well-being, whilst monitoring the impact of the drug.

The real significance of data generated by wearable devices is however not just the basic metrics of step-count, blood pressure, etc. The data has the potential to become much more significant when aggregated and integrated into a comprehensive model of patient well-being. Analysis of data points could for example provide perspectives on clinically significant changes in activity, blood pressure or sleep patterns, which might include correlation with mood changes, depression or other neurological changes.

This information could be of critical importance for companies involved in the development of drugs with potential side-effects that might impact on the subjects' mental health.

Given the above potential benefits, it is not surprising that there are numerous examples of wearable devices under development for use in clinical studies:

- The Zio XT Patch by iRhythm is a patch that detects abnormal heart activity and has FDA approval[6].
- Abbott has developed the Freestyle Libre Flash Glucose Monitoring System, a wearable skin sensor with regulatory approval to be sold in the United States and Europe[7].
- Glucowise are developing a non-invasive glucose monitor, which is a skin sensor that can be positioned between the thumb and forefinger to take an accurate blood glucose reading as required[8].
- Dexcom have developed a CGM (continuous glucose monitoring) app which connects to a dermal implant with a tiny wire and eliminates the need for finger sticks[9].

Current clinical studies

There are currently over 300 clinical studies involving the use of wearable devices for monitoring clinical parameters, many of which are studying the use of the wearables themselves.

- In 2014, Novartis established a broad collaboration with Qualcomm Life to use the latter's 2net™ as a global connectivity platform to collect and aggregate medical device data during clinical trials. The first study was an observational trial to collect a range of biometric data from COPD patients in their homes, related to the use of the Breezhaler™ inhaler device[10].
- In 2016, GSK became the first major pharmaceutical company to use a medical research app developed through Apple's ResearchKit in a study of how disease affects the lives of 300 rheumatoid arthritis patients in real time over 3 months[11]. This study simply gathered data on joint pain, stiffness, fatigue and mood, and specifically mobility to gain insight and learn more about the disease.
- The epileptic seizure study sponsored by John Hopkins University uses the Epiwatch app, also available through the Research Kit from Apple. Epiwatch provides participants with the ability to track the onset and duration of epileptic seizures in real time by activating the accelerometer and heart rate sensors at the onset of a seizure, whilst simultaneously alerting a nominated caregiver.
- Sage BioNetworks and the University of Rochester are currently collaborating in a clinical study in Parkinson's Disease that uses a simple app, mPower, which can assess physical and mental symptoms through digital interaction with the smartphone[12].

Other studies in Parkinson's Disease use a range of sensors to measure symptoms such as tremor, balance, gait, memory and some vocal characteristics to provide a more complete picture of disease progression. For example Kinesia is has developed a subject-worn finger sensor and tablet app to objectively measure specific motor tasks related to symptoms[13]. The dosage of drug (rotigotine) can then be adjusted through evaluation of the data generated by the wearable device.

In separate developments, the UK's NHS recently announced a multi-million pound investment in digital health, including significant funding for remote observation of patients. A number of test-bed studies within the organisation have also been announced, which utilise remote monitoring technologies and app-based support services to provide information on patient well-being. By 2020, it is hoped that a quarter of patients with long-term conditions such as hypertension, diabetes and cancer will be able to monitor their health remotely.

Potential problems

There are of course a number of significant problems associated with the widespread use of wearable technology in clinical studies.

- Most significantly, the devices themselves have an uncertain status from a regulatory perspective, since most technology is still seen as a consumer product. In the States, while the FDA has established guidelines that define and regulate mobile medical devices[14], there is little or no guidance for the use of wearable devices in clinical trials.
- The amount of data collected by continuous monitoring of vital signs in patients may become overwhelming, with requirements for data storage posing significant logistical hurdles for CROs, requiring remote storage or upgraded computer systems.
- Processing and analysis of this abundance of data in order to create meaningful conclusions will create its own particular problems. However the pharmaceutical industry is becoming increasingly adept at utilising and processing big data from a variety of different sources[15], suggesting that appropriate systems will evolve in time.
- Data security and data ownership are also legitimate concerns for many patients[16].
- A further concern is data accuracy and validity. Although the accuracy of devices is rapidly improving as the integral technology is further developed, there is still a need for the data collected to be validated in order to receive FDA approval.

However if these concerns can be alleviated, wearables represent a step-change in clinical

research efficacy, with huge potential benefits for the clinical trial industry.

Future trends

There is good evidence that the use of wearables and sensors in clinical trials is on the rise, and the information being generated by the current crop of clinical studies is likely to generate new insights into a range of disease states. The possibility of collecting swathes of additional lifestyle data and then integrating that information into a more holistic picture of patient health and response to medicines may improve the chances of early regulatory approval. Similarly if the aggregated data can provide a comprehensive picture of improvements to patient well-being, then it may be possible to establish a firmer case for reimbursement.

The pharmaceutical industry is by nature a conservative industry, due in part to the strong regulatory oversight provided by organisations such as the FDA. As a result, despite the great interest in the area, the use of wearable technology to study and understand physiological changes caused by illnesses or their treatment has arguably lagged behind other industries. However as the benefits of wearable devices become clearer, and as pharmaceutical companies continue to face ever increasing cost and time pressures, more technology companies are likely to enter the clinical research space and drive the utilisation of wearables. Accordingly, the majority of pharmaceutical companies and CROs plan to incorporate digital health technologies into their clinical studies over the next five years[17].

The increasing use of wearable devices is likely to lead to the emergence of unexpected and interesting applications which will further enhance the effectiveness of clinical studies, whilst at the same time driving down costs for drug development. If the issues around data validity, security and analysis can be overcome, then the use of wearable devices to measure clinical outcomes and monitor patients will make them an invaluable tool in clinical trials. As the technology develops, the aggregation and integration of data derived from wearable devices together with clinical information from more traditional sources will undoubtedly begin to radically transform our understanding of disease pathology and treatment options, to the benefit of drug developers, payers and patients alike.

Sources

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