Notable Opportunities and Challenges of Wearable Technology in Clinical Trials

PEER REVIEWED

Consumer-grade wearable devices offer the potential to continuously monitor many different physiological measures of health and fitness as individuals go about their daily routines. For a clinical trial, this could provide valuable insights between hospital visits, potentially enhancing the understanding of treatment response, delivering a rudimentary early warning system, providing objective measures of more subjective outcomes or even provide efficiencies in trial conduct.

Before the widespread adoption of such technology in clinical trials, however, there are several significant challenges from data access and interpretation to clinical validation. In this article, we offer insights into our experience and some of the specific challenges that exist, focusing on the collection and analysis of data including the interpretation and generation of meaningful clinical insights.

Wearable Activity Trackers

There is considerable discussion around the use of patient-generated data in health research and clinical studies, particularly from wearable activity trackers. Since around 2013 there has been a large increase in sales of consumer-grade activity tracking devices and it is estimated that over 22% of adults in the US alone will wear a smart watch for at least one month in 2019 according to eMarketer[1], and the smart wearables market is predicted by Forbes to double by 2022 (October 2018)[2]. This popularity gives rise to a potentially under-utilised data source for clinical research.

During a clinical study, a patient is often closely monitored with a detailed analysis of their blood, vital signs etc. at specified timepoints, or visits to the clinic. However, with basic activity trackers providing accelerometer-based activity data and more sophisticated models capable of also monitoring heart rate and other features, these devices have the potential to provide insights into an individual's health, fitness and sleep 24 hours a day, seven days a week. During a clinical trial, this would provide valuable information for each patient between clinic visits. Furthermore, there are subjective events that can be both under-reported and difficult to measure, for example fatigue, novel endpoints, or general wellbeing. From a physician's perspective, a greater awareness of these events may help them with appropriate interventions or advice and more generally, this information could be important in defining the tolerability of new treatments from a patient's perspective.

Limited Evidence

Despite the potential around wearables, there is limited indication of how the data from consumer-grade devices might be used in clinical studies. Although wearable activity trackers are gaining traction in clinical trials, most focus on their use either as an intervention (e.g. in weight loss or behavioural studies) or in comparing consumer-grade with medical-grade devices. There is potential for clinical teams to extract value from this data alongside the routinely collected data at visits. It is worth noting that there is much debate around the use of consumer-grade devices in clinical research and the accuracy and validity of most devices has not been verified formally. As a result, their use within such research should be with the appropriate level of caution/awareness.

While consumer-grade activity trackers may have the potential to provide insights into patients' general health and fitness and overall wellbeing between visits, there are, however, several challenges associated with the access to and utilisation of this type of data, for instance:

1. Data connectivity: accessing and extracting the data for an individual.
2. Types and frequency of data reported.
3. Missing data (including non-wear time).
4. Generating meaningful insights from the data.
5. Data privacy and security.
6. Clinical validation.

Despite these challenges, consumer-grade wearable data may provide benefits during clinical trials:

1. Valuable information alongside the standard clinical data collected during a clinical trial.
2. Improvement in recruitment because patients are actively involved in clinical research.
3. Better quality of the findings.
4. Greater impact because it empowers patients to donate their own data toward decision-making about their own health. This may have a positive impact on the patient's own experience of a clinical study and may improve the dialogue between patient and caregiver.

Effective extraction, processing and creating actionable health-related insights could potentially enable continuous monitoring of individuals outside of the clinic. This could empower the patient, as they will retain control over the additional information and data they provide to the clinical study team.

Four Key Challenges

There are many challenges in utilising the data from consumer-grade activity trackers as suggested above. The clinical validation is extremely important and should be a key consideration if planning to utilise these consumer-grade devices during a clinical trial as well as the data privacy and security. For the remainder of this article, however, we will focus specifically on the practical challenges around the data and the workflow; from data access through to meaningful analysis.

Challenge 1: Data Connectivity Challenges with Wearables

Within data connectivity for wearables, there are two areas of concern. The first is what data the manufacturer will allow you to access, and the second is how to create a workflow for the secure transfer of the data from the device for analysis.

We conducted a small study where we provided full instructions so that volunteers could download their data from their device account to a secure server. They were able to select which data to

download and all participants opted to share their sleep and activity data in its entirety. This would not be a feasible approach in a larger study. The particular device used in this study provided data on a daily summary level - it would have been possible to access intraday data through an application programming interface (API), however this would be subject to review by the device company.

Our approach for this study was simple – volunteers would share their daily data with the investigators. Careful consideration would be required if this approach was scaled to a larger clinical trial, especially around how, with appropriate consent, an individual's data would be securely transferred and linked to existing data, all the while ensuring anonymity. Furthermore, consideration needs to be given to the appropriate, country-specific governing laws, for instance GDPR in the EU and the differing US laws depending on the grade of the device, be they medical grade or consumer grade.

Challenge 2: Types of Data Reported

Although activity trackers essentially measure activity via an accelerometer (and, with some devices, a heart rate monitor), there are several marked differences in the available data from the various devices on the market.

There are also limitations in the use of such data, such as data being summarised as daily values, the definition of activity and sleep relying on the devices interpretation of the heart rate data and often the lack of any granular accelerometer or heart rate data. It is imperative to consider these device-specific limitations when choosing which data should be included for analysis.

Challenge 3: Missing Data and Non-wear Time

There are two types of missing data to be aware of with activity trackers. The first challenge arises where some data for a given day is reported, but the granular data is unavailable. An example is sleep data: the time to bed and wake-up times may be reported; however, the sleep stages may be missing. Alternatively, we may have activity data for each day but no sleep data at all, suggesting an individual removed their device at night.

The second challenge around missing data is non-wear time, where, for example, a device is removed for a short period of time during the day. Many wearables do not directly report non-wear time, however from the data it may be possible to approximate non-wear time per day for an individual based on a calculation over a 24-hour period. Such calculations can be based on the two assumptions: (1) an individual does not wake between the sleep start and end time (this, of course, is not strictly correct as individuals could wake in the night and remove the device for a time and then put it back on) and (2) If the device reports the number of sedentary minutes for a given day to be 1440 (the total number of minutes in a day) then it was assumed the user was not wearing the device.

In the study we conducted, we looked at the non-wear time over the month. We found that overall, the total non-wear time was low. Questionnaire results suggested that most individuals only removed the device for charging and showering, with some choosing to not wear the device for prolonged periods such as for particular social occasions or to sleep.

Analyses should factor in non-wear time and missing data. Thought should be given to what missing data there might be, how it will be calculated or detected and how to deal with the missing data. Certainly, it is important that the amount of missing data be made clear to those who are interpreting the data, along with any assumptions that have been made.

Challenge 4: Generating Meaningful Insights Directly from the Device Data

Another major challenge in the use of wearable devices is around the interpretation of the data by clinicians. The volume of data generated by wearables could potentially be overwhelming to a physician or a clinical study team. For instance, many trackers can measure heart rate continuously over a 24-hour period, which over the course of a clinical study is a lot of data points. There is still much to be done in this area in understanding how this data can be translated into something usable by the clinical and/or study team. Moreover, it is important to consider what medical intervention would result from the interpretation of such information.

It is known that sleep is an important measure of health[3], activity can improve aspects of our wellbeing[4] and physical activity impacts the overall quality of sleep[5]. If we look at the data generated at the single patient level it may be possible to look at changes in the sleep of an individual over time or a decrease in activity levels. The result from such insights may lead to an enhanced conversation between patient and caregiver with two-fold impact; firstly, the patient may feel more reassured that they are contributing to the consultation and secondly, there may be a medical intervention or a specific piece of advice the caregiver can provide that may help that patient. It must be noted that if the devices being utilised are consumer-grade devices, consideration must be given to the validity and accuracy of these measurements.

Examine the Trends

A clinical study team may be interested in the data at the level of a population and want to consider potential trends in the data to provide meaningful insights. There are many ways to look at the data, such as the non-sedentary time on each day of the week. In our study with healthy volunteers, activity levels increased on the weekends, as one would expect. Translated to a clinical study, this sort of information could be utilised to study trends in the days following dosing, for example the general activity levels post-dose across the trial population, which may provide insights into tolerability.

More generally we can look at the association between activity and sleep. There is no consensus on how to measure sleep quality; in our study, we applied the approach of Valenti *et al.*[6] and defined sleep quality as the time spent in REM and deep sleep divided by the total minutes asleep, and looked at activity vs. sleep quality.

As mentioned previously, the volume of data from activity trackers can potentially be very large and it isn't necessarily clear how a caregiver may consistently extract value from such data for an individual subject. It may be beneficial to use the activity/sleep data as an indicator of other health events. One potential application could be in the indication of a general sense of a patient's wellbeing, which in turn could provide insight into drug tolerability.

Wellbeing is subjective, sometimes relying upon a dialogue between patient and caregiver. One approach used to measure wellbeing is a validated questionnaire, completed by the patient, which relies upon recall from a previous fixed duration. One such questionnaire is the WHO-5[7,8], which is a short self-reported measure of current mental wellbeing over the previous two-week period. During the study we conducted, we asked participants to complete an online version of the WHO-5. Although not a large enough sample size to be statistically meaningful, it provided some preliminary data on any possible association of activity tracking data to wellbeing.

Conclusion

Consumer-grade wearable devices offer the potential to monitor an individual 24/7 as part of their daily routines, away from a hospital setting and include a myriad of physiological measurements from brain activity through to temperature. Although there are several clinical trials utilising wearable devices, often as an endpoint or as an intervention, researchers are only just beginning to understand how to extract value from such rich data to generate clinical insights. For instance, digitally-collected data from a wearable device may be transformed, through mathematical models and machine learning, into indicators of health outcomes. It may be possible that characteristics in an individual's activity or sleep could form an objective measure of their general wellbeing or fatigue levels, which could then be used to inform their physician and/or provide insights across the study around general tolerability.

The role of wearable technology in healthcare and clinical trials is promising; the potential applications are diverse including enhancing our understanding of responses to treatment and efficiency gains in clinical trial conduct. However, there are significant challenges and the community would benefit from the regular exchange of learnings and experiences to facilitate the development of best practices around the deployment, collection, standardisation and analysis of such data for validated clinical applications.

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