Editorial

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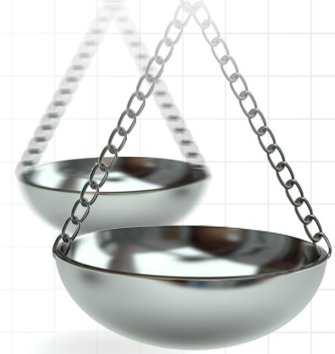

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The use of digital technologies to collect patient data in outcomes research

"Leveraging bring your own device, smartphone sensors and shareables in our studies should be encouraged. It has the potential to significantly reduce the proportion of subjects providing data on paper and limit the associated paper data management processes..."

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Real-world evidence (RWE) research is increasingly important as a component of biopharmaceutical product development and commercialization. Outcomes measures supporting RWE come from a variety of sources and, in prospective evaluations, data collected directly from patients is a valuable component. However, collecting data from participants in observational research and RWE studies has specific challenges when compared with clinical trials in pre-approval phases. In Phase II–III, for example, it is common to provide mobile devices and wearable technology to patients to collect clinical outcome assessments (COA) for the duration of the study observation period, and to impose a frequent and rigid schedule of protocol-mandated clinic visits.

Observational studies, however, often involve high numbers of patients and observe patients for longer periods of time, sometimes a number of years. Further, the opportunity for data collection is less frequent as it is driven by standard of care treatment regimens (e.g., monthly or quarterly). These properties mean it is often financially and logistically infeasible to provision hardware to patients for self-report of outcomes, and not practical to expect frequent assessment. While surveys and questionnaires can be used to collect self-reported outcomes data, paper collection of patient-reported outcomes data has known limitations in data quality and integrity [1]. In this editorial we explore the use of digital technology to collect outcomes data in observational and RWE studies.

Bring your own device

The ability to develop and deploy consumer apps has been accelerated by the open development platforms offered by Apple®, Android® and others. Concerns about using bring your own device (BYOD) to collect patient-reported outcomes in clinical trials has focused mainly around data security, and concerns that displaying validated instruments on devices of varying screen sizes and resolutions may affect the instrument measurement properties and therefore question the integrity of data collected in this way. Recently, however, evidence supporting the conservation of instrument measurement properties across paper and different devices

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has been summarized in a number of meta-analyses of published equivalence studies [2,3].

In most territories, Apple and Android dominate the mobile device market. In the USA, for example, smartphone subscriptions for Apple and Android were 43.6 and 52.8% in 2016, with the remaining 3.6% taken up by Microsoft® and Blackberry® [4]. There are a growing number of direct-to-patient research studies using Apple ResearchKit [5], but might development on just one platform introduce a level of bias into the sample and affect generalization of results? There is some evidence that in some circumstances it might. MapBox (DC, USA), for example, provide maps showing the geolocation of Twitter activity from mobile devices [6]. By presenting tweets from Apple and Android devices separately it can be seen that in some US cities, for example, Apple and Android usage appears associated with sociodemographic differences, with Android incidence more prevalent in less affluent areas. Collecting data using just one of the two major platforms may, in these cases, skew the sample of patients to one or another sociodemographic group. Of course, non-smartphone users represent another group that may need to be accounted for in other ways, such as paper surveys.

> "While validation work is needed to measure the reliability and understand the interpretability of end points captured in this way, the potential is clear."

BYOD for patient-reported outcomes

Collecting patient-reported outcomes using an app that the patient is able to download from an app store onto their own mobile device provides the opportunity to collect robust COA data with strong validity and integrity. For studies requiring regular measurement over a short time period, this provides a good solution for patients with suitable devices, reducing the amount of paper data processing and improving study data quality. Apps that provide additional value and engagement for the patient may be particularly successful in collecting regular and timely COA data. The 100 for Parkinson's study provides a good example [7]. This study recruited over 4,000 patients via social media and advocacy groups over a 5-month period. Patients were able to record data every day for 100 days to track their condition and receive medication adherence reminders. In addition to validated instruments, such as the EQ-5D-5L, the app asked patients to rate a number of symptoms on a daily basis. In addition to the five symptoms defined by the study, patients could select and track an additional five symptoms that were most important to them. While the study was not prescriptive on how often symptoms should be recorded, this engaging approach was successful in achieving measurements numerous times per week for most participants.

In studies with long study observation periods during which the mobile platform may change considerably, and in studies requiring only infrequent assessment, the use of an app may not be optimal. In such studies, COA platforms that enable a number of different collection approaches are valuable, such as the use of electronic survey methodologies. Email can enable the push of rich information and provide links to secure web forms to collect outcomes data. With all such approaches, the selected solution should include appropriate data privacy and data protection safeguards.

Leveraging smartphone sensors

Due to the increasing miniaturization of sensors and circuitry, smartphones have been able to leverage multiple inbuilt sensors to enhance user experience and provide other features. For example, tri-axial accelerometers are useful in determining the spatial positioning of the smartphone and thus enabling the screen to re-orientate when the handset is rotated. More recently, novel application of these inbuilt sensors has enabled new and inventive uses for the smartphone in the area of health and wellness [8]. This offers an opportunity to collect novel, objective health outcome measures in prospective studies.

A compelling example is the application to study Parkinson's disease developed by Roche in collaboration with academic research groups [9–11]. This Android app leverages a number of sensors and components in the patient's own smartphone to measure aspects of health status and symptomatology while conducting a number of short performance tasks. Tasks include a phonation test to measure voice degeneration, simple tests of balance and gait using the accelerometer to measure sway and stepping, a finger tapping dexterity test using the smartphone touchscreen and tests to measure tremor using the device accelerometer while the patient holds their smartphone with arm extended for 30 s. Frequent objective measurement is valuable in the assessment of Parkinson's disease where symptoms important in optimizing treatment may not be observed every day or during routine clinic assessments.

While validation work is needed to measure the reliability and understand the interpretability of end points captured in this way, the potential is clear. Smartphones offer a unique way to measure objective health outcomes in large populations without the need to supply wearables or other devices. We see this potential in the growing number of applications launched using Apple ResearchKit that includes performance

tests to collect objective outcomes longitudinally. Examples include the 6-min walking test (MyHeart Counts [5]), simple cognitive function tests (Concussion Tracker [5]) and the daily total number of steps (Glucosuccess app [5]).

Objective outcomes: wearables & shareables

Consumer wearable platforms often provide the capability to share personal health data. Fitbit (CA, USA) and other consumer activity trackers, for example, enable app developers to access activity data with the user's permission. In such cases, a study app may request permission to access wearable data and this authorization, when granted by the user, is managed through the web service connection of the wearable device platform. This provides the opportunity to collect additional outcomes data using wearable devices. However, as fewer people own consumer wearables there is less potential to leverage wearables in a BYOD setting in the same ways as mobile devices.

There is another approach however; an emerging area that leverages free-to-access technology, sometimes described as 'shareables'. In the USA, for example, the largest provider of personal health kiosks, Higi (IL, USA), provides over 11,000 stations in various supermarket, pharmacy and other retail environments. These are free to use by the consumer, who is able to measure and track their own health outcomes including heart rate, blood pressure, body composition and body mass index. Many users will find a health station in a location close to their home, work or where they shop regularly making possible regular longitudinal measurement. In the same way as consumer wearables, these platforms enable users to 'opt in' to share their data with specific programs or studies. The data from opted-in subjects can be accessed via web services and this enables research studies to access and track robust objective measures in consenting patients without the need to supply wearable technology. As we see these networks expand geographically, and increase the range of assessments they are able to measure, shareables offer an increasingly viable opportunity to collect objective outcomes measures in observational and RWE studies.

While not all patients in an observational or RWE study may own a suitable mobile device, the proportion is high in most territories. In a study recently conducted by ICON, over 95% of participants (n > 150) were willing to use their own mobile device in a research study (Byron B, Unpublished Data). Leveraging BYOD, smartphone sensors and shareables in our studies should be encouraged. It has the potential to significantly reduce the proportion of subjects providing data on paper and limit the associated paper data management processes, and to improve the richness, quality and integrity of data we collect and report in RWE evaluations.

Financial & competing interests disclosure

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