Robin Robinson

mHEALTH TOOLS
Can Streamline Clinical Trials

Studies show that mobile tools increase trial engagement while lowering costs.

You may be holding the most important medical devices of the future in your hand: a smartphone and a mobile app. As the clinical trial space explores ways to leverage the personal and ubiquitous nature of mobile phones, it could also find a solution to two of its biggest challenges: patient engagement and the high cost of recruitment. The integration of mobile technology in clinical trial design is a fast, efficient way to align patients' needs with study objectives.

Mobile apps are being created for use in clinical trials, connecting every patient with a smartphone to clinical trial information, participation opportunities, and tracking and monitoring capabilities. Mobile apps connect participants easily to electronic data capture and clinical trial management systems, as well as imaging and reference sites. Studies show that this extreme connectivity can improve participant compliance and overall patient outcomes.

For example, in Maryland, researchers conducted a cluster-randomized trial using a mobile phone to personalize behavioral intervention for blood glucose control to test whether adding mobile application coaching and patient/provider Web portals to standard diabetes management would further reduce glycated hemoglobin levels in patients with type 2 diabetes. The Mobile Diabetes Intervention Study randomly assigned 26 primary care practices to one of three stepped treatment groups or a control group (usual care). A total of 163 patients were enrolled and included in the analysis. The mean declines in glycated hemoglobin were 1.9% in the maximal treatment group and 0.7% in the usual care group, a difference of 1.2% over 12 months. The study concluded that the combination of patient behavioral mobile coaching with blood glucose data, lifestyle behaviors, and patient self-management data individually analyzed and presented substantially reduced glycated hemoglobin levels over one year.

Pharma is just beginning to realize this benefit of how mobile technology can optimize clinical trials. According to Marc Perlman, global VP, Oracle Healthcare and Life Sciences, mHealth technologies hold great potential to accelerate trials, reduce risks, and drive down costs.

"mHealth technologies enable continuous monitoring that can have an immediate positive impact on patient safety," he says. "With vast and accurate information streaming in real time, researchers can more quickly identify potential adverse events or side effects, such as changes to heart rate, heart rhythm, blood pressure, or sleeping patterns, after taking a medication or therapy and take action to intercede. This capability also has promising application in post-market surveillance."

Access to real-time information can support adaptive trials, providing early indications of changes that might need to be made to protocol, sample size, or trial scope, Mr. Perlman adds. Similarly, trial sponsors can have earlier insight into a therapy that is performing better than expected, which would accelerate the delivery of life-saving treatments to market.

The amount and quality of data captured from a tap of the finger on a smartphone is a virtual goldmine for pharma, especially when it comes to patient recruitment in clinical trials, says Jeff Meehan, chief commercial officer at MD On-Line.

"Pharma companies today are reaping the benefits of technology in healthcare — from the immense amount of data available through EHRs, practice management systems, and electronic claims, and making smart connections to doctors and patients or using technology to get face-to-face with customers, the ability to use technology to expand their reach and increase efficiency is highly appealing," he says. "This use of technology has never been more evident in playing a key role in the area of patient recruitment for clinical trials. Slow patient recruitment and retention for trials can mean hundreds of millions lost for companies due to the lag time in product approvals. However, new ways of targeting doctors and patients for trials has emerged using real-time clinical data."

For example, new solutions are providing physicians immediate access to information on which clinical trials are currently in progress in their area. These tools can be embedded in a physician's billing and coding data to enable the physician to know exactly how many patients in the practice qualify for trials based on inclusion and exclusion criteria and why these trials could benefit patients.

DR. SUSAN DALLABRIDA ▪ *PHT*

"Device integration is a pivotal next step in mHealth technologies for clinical development."

"As many in the industry are aware, finding the right candidates is often referred to as the biggest bottleneck in medical research," Mr. Meehan says. "By simply leveraging the technology that's right in front of us, we're able to save precious time during the clinical trial process. This allows researchers to focus on what matters most — the development and approval of life-saving medicines and treatments."

On the patient side of things, there are several apps that help them find and sign up for

appropriate clinical trials right from their smartphone. Novartis Oncology developed a mobile app, Clinical Trial Seek, where patients and physicians can look for cancer trial information.

With mHealth technology like this at work, pharma companies can keep clinical trial subjects more fully engaged, says Jonathan Javitt, CEO and vice chairman of Telcare, a provider of mobile diabetes management solutions. Additionally, using mHealth technology, study protocols can be set up with flexible schedules that can be fixed, randomized, or event or self-triggered. Schedules can be set up for hourly, daily, weekly, or monthly events. Surveys can consist of single quick questions or complex instruments with conditional responses. Diary entries can be established for study biomarkers and these can be either initiated or validated by other external devices that also report to a control center. Educational programs consisting of podcasts or other Web-based content can be scheduled, shared with professional and family caregivers, and even tested within the system, he adds.

Simple Web management of content allows researchers to insert and change medication schedules and reminders, customizable surveys, podcast-style education modules, and intervention activities on individual smartphones quickly and easily. Data are captured in real time and other study activity is tracked.

"Noncompliance can be identified and action taken to quickly bring a trial participant back into compliance," Mr. Javitt says. "Also,

JEFF MEEHAN ▪ *MD On-Line*

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there is benefit in knowing in real time when and if a dose was taken, as well as knowing what the other treatment markers are before, at, and after the dosing."

New mHealth Technology in Clinical Trials

Mobile phones aren't the only tool enhancing clinical trial effectiveness. Bio patches, wireless sensors, non-invasive vital sign solutions, even ingestible technology are all enabling the real-time, continuous monitoring and data capture for patients on or off-site.

"We are beginning to see some interesting mHealth technologies emerge for the clinical development space," Mr. Perlman says.

For example, Proteus Digital Health provides an FDA-approved ingestible event marker and sensor that captures precise information about medication ingestion, dose timing, and physiologic responses and behaviors that send the digital health information to a patient's smartphone.

The ingestible event marker sends a signal recording the time the patient took a pill and its unique identifier. A sensor worn on the skin captures continuous readings of the patient's heart rate, temperature, activity, and rest patterns. The solution can collect more than 5,000 data points per minute.

There are many applications for integrating physiologic monitoring data with mHealth solutions. Examples of these include Peak Expiratory Flow (PEF) meters, glucometers, activity meters, measures of vital signs, and body weight. As simple as these home measures are to record, they are often pivotal indicators of a change in health status. Activity monitoring is one of most important measures for health for patients with certain respiratory diseases, according to Susan Dallabrida, Ph.D., VP of clinical science and consulting at PHT.

For example, for people with heart disease, small changes in body weight can tell a physician if the patient is likely accumulating fluids and potentially headed for heart failure.

"The advantage with mHealth solutions is that this technology provides a way for physiologic data to go directly to the clinician in real time, so it enables real time monitoring and adjustments in clinical care," Dr. Dallabrida says. "We're seeing a lot more monitoring of this type and integration of physiologic measures with our devices. Coupling physiologic values with subject PRO measures gives us a much more complete understanding of the patient's health status. This coupling enables the physician to make the optimal adjustments in clinical course and education and consequently, positively impacts healthcare in a patient centered manner."

Device integration is a pivotal next step in mHealth technologies for clinical development, Dr. Dallabrida adds.

"We see this across all therapeutic areas," she says. "We're talking about device integration that couples some readout about the subject's physiological parameters with the mHealth device and the PROs collected."

Studies show that when patients get a glucose reading from their glucometer and are instructed to report the value on paper they tend to misreport the value and most commonly distort the glucose value such that it is altered to be in the normal range. In addition, on paper, patients have been shown to miss and create values. That issue coupled with the diminution of the actual amount and extent of hyperglycemia and/or hypoglycemia provides misinformation to the physician on the patient's health status and can translate into suboptimal care.

"It's clear that with non-integrated technologies we've been missing true blood glucose values," Dr. Dallabrida says. "This has become a big topic among sponsors that are now using mHealth solutions and are pulling in more data than they expected based on historical expectations derived from studies done on paper."

With something as simple as an accurate record of blood glucose values, the clinical care can be improved and optimized for patients with diabetes. Studies have shown that diabetes patients who keep track of their blood glucose values electronically using mHealth solutions have better kidney health than those who do not using the technology and those using a paper notebook.

Benefits of Mobile Apps in Clinical Trials

Using mHealth to better manage clinical trials can help ensure trial subject retention, avoid journal errors and memory failure, provide better information, allow for intercessions earlier, complete milestone and market entry when the trial results merit approval, Mr. Monroe says.

mHealth technologies can also benefit clinical trials by improving safety and visibility into protocol adherence, Mr. Perlman says.

"They offer new potential for validating and improving protocol adherence — an area that continues to challenge clinical trial sponsors and managers," he says

Continuous monitoring, made possible through mHealth technologies, can enable researchers to confirm treatment adherence with near absolute certainty, which is not possible today. As a result, study sponsors and managers could more accurately determine efficacy as they can filter out non-adhering patients. There is also a link to improved safety as trial sponsors could quickly identify potential adverse events or side effects, such as changes to heart rate or rhythm, blood pressure, or sleeping patterns, after taking a medication or therapy. Additionally, benefits can also be realized by near real-time analysis of the data to determine common, unintended benefits of the protocol as well.

"In addition, continuous monitoring can facilitate subject recruitment and, ultimately, shorten the length of a trial," Mr. Perlman says. "If a participant is not adhering, trial managers could drop them quickly, yielding earlier insight into how many subjects will be required to complete the trial."

Continuous monitoring can also help to improve participant retention as recording critical data and adherence will be more convenient, requiring less travel, or face-to-face interaction. Further, the ability to automatically upload data to the clinical data management system would help eliminate manual input into an electronic case report form — driving new levels of study accuracy and efficiency.

mHealth tools can bring about cost savings as well as accuracy, Mr. Javitt says.

"Trials that require the use of fingerstick glucose meters are particularly expensive because of the extreme difficulty associated with getting patients to test blood sugar and log the results," he says. "With mHealth technology, clinical trials organizations have found a doubling of adherence to glucose testing. Moreover, study monitors can identify and contact patients who miss tests in time to obtain patient adherence and minimize study protocol violations that damage the integrity of the entire study."

Thus, at one level, mHealth technology reduces per-patient data collection and study monitoring costs, while improving study integrity. In the case of diabetes, however, there may be a more profound impact of mHealth technology. While new drugs are frequently able to prove non-inferiority, compared with marketed brands, this is rarely sufficient to achieve economic success of a new, innovative drug, particularly when the market standard is nearing the end of its patent life. Pushing the envelope in overall A1c control is challenging and there is little prospect for new drugs to demonstrate superiority in this regard.

"However, if fingerstick glucose results can be obtained with sufficient regularity, the potential exists to demonstrate meaningful reductions in hypoglycemic events and glucose fluctuations – parameters that cannot be ascertained by A1c alone," Mr. Javitt says. "Since hypoglycemia is the main cause of short term hospitalization, morbidity, and even death in diabetes, any pharmaceutical company that is able to demonstrate superiority in this parameter, while maintaining non-inferiority in A1c will have a blockbuster drug." PV

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