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Patient and Clinician Reported Outcomes in Clinical Trials

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ePRO/eCOA Grows with Eye Toward mHealth Future

Lisa Henderson

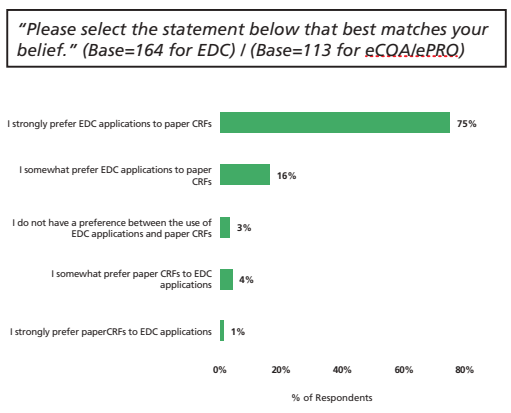
Recent industry surveys show clinical trials professionals look toward improved technologies.

Using the latest industry data regarding the perceptions and attitudes around ePRO/eCOA and the use of mHealth to reap benefits in clinical trials, we uncovered some trends:

- Industry is turning away from paper.
- Mobile health technologies use will increase in clinical trials.
- Security concerns still exist in the electronic world.

Let's turn first to Industry Standard Research's EDC and eCOA/ePRO Market Dynamic and Service Provider Performance report. In its survey of 166 respondents from sponsors, CROs, and sites, it noted the increasing acceptance and use of EDC and eCOA/ePRO technologies among sponsor companies and CROs. Andrew Schafer, president of ISR noted, "Findings show that 91% of respondents exhibit a greater preference towards EDC than paper CRFs, a preference increase of almost 15 percentage points from two years earlier."

Figure 1: EDC Applications vs. Paper



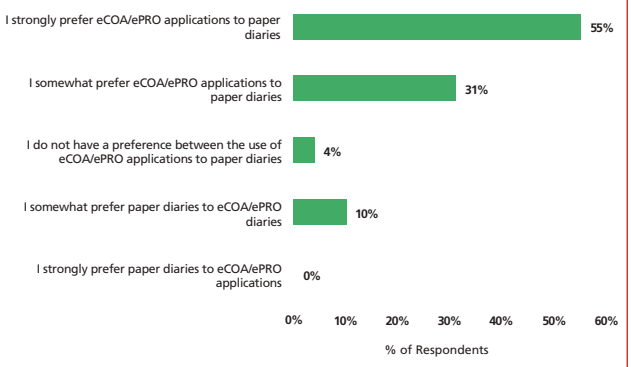
Source: ISR's EDC and eCOA/ePRO Market Dynamic and Service Provider Performance (2015)

And in the area specific to ePRO/eCOA, Schafer notes, "86% of respondents report a preference of eCOA/ePRO over paper diaries compared to a 61% preference in 2013." Schafer also added, "Such a vast difference in the preference between electronic and paper-based methods not only indicates a realization of the potential benefits gained through the use of electronic technologies, but also points to a fairly clear gravitation away from paper-based methods.

Schafer said that this trend has several implications for both sponsor/CRO companies and technology providers. For providers, Schafer advised they be aware of growing demands for technological services within the clinical trial arena. "Prepare for additional adoption of your services and possible expansion of your sponsor's preferred provider list," he said.

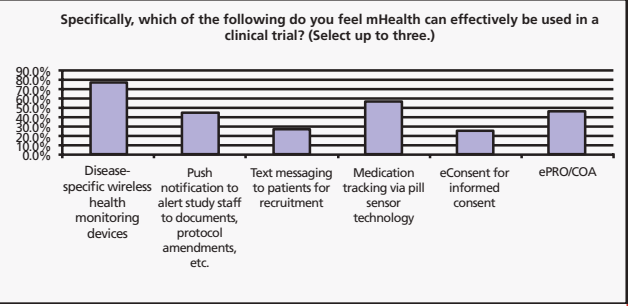
For sponsors and CROs, Schafer suggested they have an understanding of the breadth of providers available in their use of data collection technologies. The ISR report includes information about providers, including their area of focus.

Figure 2: eCOA/ePRO Applications vs. Paper



Source: ISR's EDC and eCOA/ePRO Market Dynamic and Service Provider Performance (2015)

Figure 3. mHealth Use in Clinical Trials



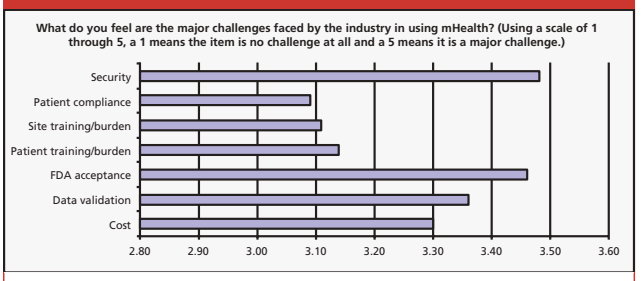
Source: Applied Clinical Trials, SCORR Marketing survey, December 2014.

mHealth and ePRO

When *Applied Clinical Trials* conducted its mHealth survey in December 2014 with SCORR Marketing, we found that ePRO/eCOA collection could be impacted by mHealth. Figure 3 shows the various ways respondents felt that mHealth could be used effectively in clinical trials. While ePRO/eCOA was not the first, it came in third behind disease-specific wireless health monitoring devices and medication tracking via pill sensor technology. What is clear is that the potential uses for mHealth technologies are around the patient—whether that is wearable technology that directly takes patient health data direct to a system, to the patient's compliance with a treatment regimen, or ePRO/eCOA direct data collection from patients regarding how they say they feel about the drug.

Technology, no matter what form it takes, has always been under security suspicions, and mHealth is no different. What asked what is the biggest challenging to industry in using

Figure 4: Industry Challenges with mHealth



Source: Applied Clinical Trials, SCORR Marketing survey, December 2014.

mHealth, the top answer was security. In a current survey on wearable technologies in clinical trials, interim results show that respondents are very concerned to somewhat concerned at 67%. Contrast this with a survey we conducted two years ago, where respondents said that cloud technologies were not secure, was listed as the second-highest concern for that technology.

To be sure, security is not limited to systems vulnerability or data breaches, but in the case of ePRO/eCOA, security concerns around the device itself. At a recent conference, ePRO decision-makers discussed their concerns around the loss of data or device or breakage of device by a patient.

In our survey, the remaining top challenges industry faces regarding mHealth in clinical trials is FDA acceptance, data validation and cost.

In this eBook, we have included articles that address these concerns and trends. Articles explore the future of ePRO platforms, technology providers' views on innovation and possibilities of eCOA in the near future, the applicability of Bring Your Own Device in the ePRO world and the book closes on a chapter regarding the growing market for patient reported outcomes outside of Phase I through III clinical trials.

What we did not discuss specifically in this eBook, but what should be clear—patient engagement is center to the use of personal devices or mobile health uses in clinical trials. While the issue of data quality and accuracy is paramount in any trial, patients increasingly have a voice in the value of a drug.

Lisa Henderson is Editorial Director for *Applied Clinical Trials*.

References

1. Industry Standard Research's EDC and eCOA/ePRO Market Dynamic and Service Provider Performance 2015. http://bit.ly/1KIUkBF
2. SCORR Marketing and *Applied Clinical Trials* mHealth in Clinical Trials Survey Report. http://bit.ly/1FG2vPO

The Future of ePRO Platforms

Alan Yeomans

The historical paths of ePRO leads us to a future of mobile platform usage not yet well travelled.

It is tempting to imagine the use of the patient's own mobile computing platform for collection of patient-reported outcomes (PROs). This would solve some of the problems faced when using the electronic PRO (ePRO) devices employed today:

- Provisioning costs (purchasing or leasing the devices to be used in the trial)
- Supply issues (delivering the devices to the sites for distribution to subjects, and collection after the subject completes the trial)
- Training (handling and use of the device by subjects and site staff)
- Maintenance and Help Desk (device-related help desk questions, replacement of faulty devices)

This article evaluates the practicality of such an approach, and the issues that need to be addressed if it is to succeed.

Present state of the art

The goal of a PRO system is to collect data directly from subjects; data used to measure the benefit of treatment or the risk in medical clinical trials.[1] Initially, this was done using a pen and paper, and patient responses were collected in the form of surveys conducted once (or a few times) during a trial and/or in the form of a patient diary, containing responses collected regularly throughout the trial.

The move toward ePRO solutions, which started in the 1990s, was fueled by a number of considerations, primarily:

- Improved compliance through the use of alarms, reminders, and date and time stamps
- Improved data quality through the use of electronic data collection and in-built data checks
- Reduced trial times due to quick access to data without requiring data transcription

Interestingly enough, cost has not been one of the primary movers. Although most companies adopting ePRO have had hopes that improved compliance, data quality, and reduced trial times in themselves would lead to cost savings, these cost savings were difficult to quantify. Indeed, often the move to ePRO involved higher up-front costs, with eventual savings being realized later in the trial process.

ePRO solutions diverged early along two paths. The simplest and most cost-effective tools have been the interactive voice response systems (IVRS), but these have had restrictions in their functionality, the user interface, and the type of data that can be collected.

In order to support the collection of more complicated data, a number of vendors developed solutions that could support entry of textual and graphical data.[2] These solutions were based on proprietary software running on commercially available electronic platforms, or "device-based applications." Initially, these solutions were based on commercially available personal digital assistants (PDA) platforms. The earliest were based on the Apple Newton PDA, followed in the late 1990s by systems using the Palm Pilot. These all used offline synchronization techniques, making it necessary to store data temporarily on the device itself, initially until the next time the patient visited the

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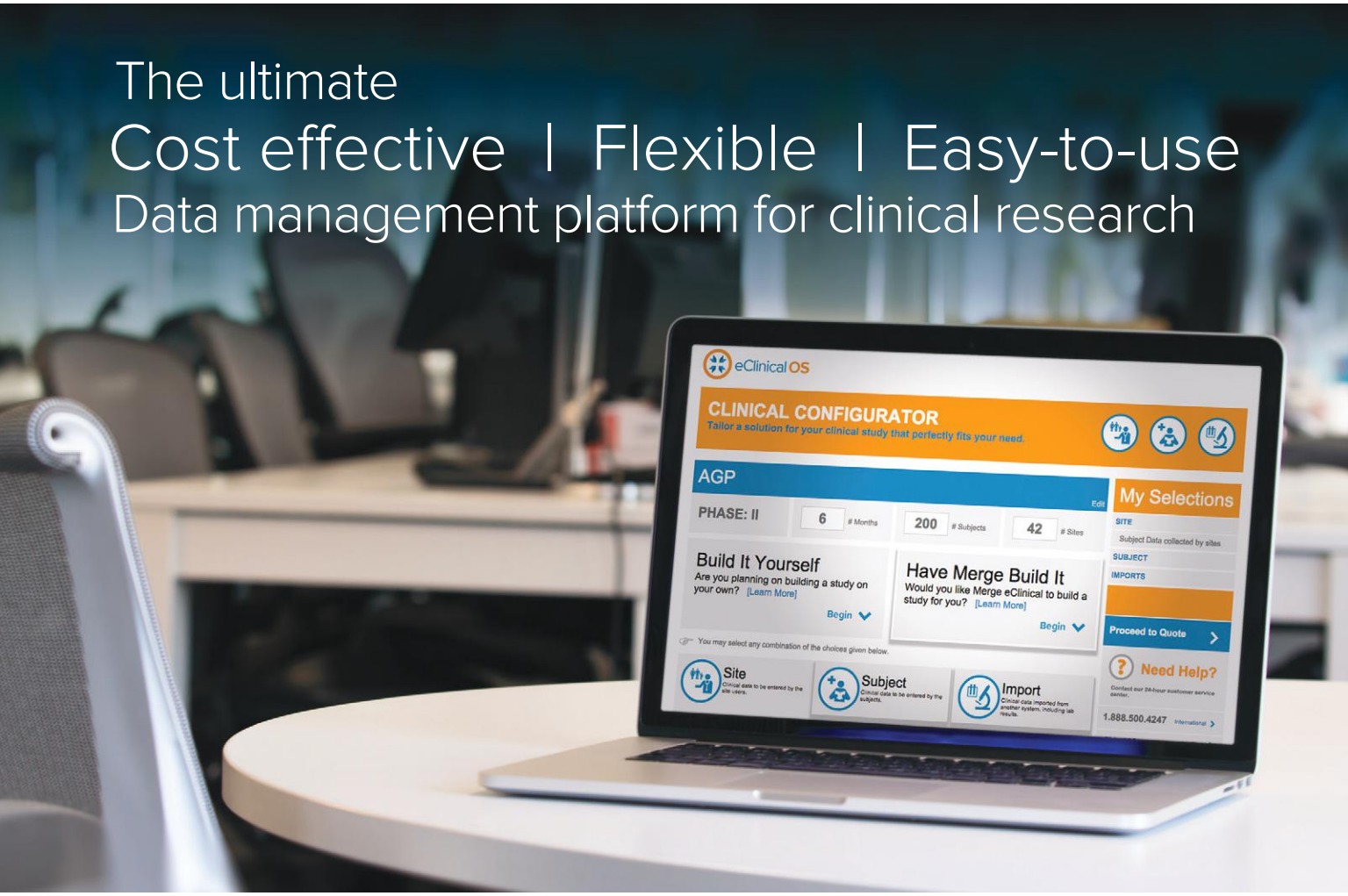

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clinic. Later on, solutions were developed that allowed subjects to synchronize remotely (e.g., from home). GSM-enabled PDA devices were introduced in the early 2000s, allowing continuous synchronization (as long as the subject was within reach of a GSM network).

The one thing in common for device-based applications is that they used proprietary software installed on a commercial platform. This necessitated supplying subjects with the devices to be used for the study in question, training them in the use of the devices, and collecting the devices from the subjects as they complete or withdraw from the trial.

Because device-based applications store the application itself and in many cases act as a temporary store for the data then there are special requirements that need to be addressed by these solutions.[1,3] The software must prevent end users from:

- Modifying the application or the data stored on the device
- Installing and using other applications that may influence the device-based ePRO application or the data collected
- Deleting the ePRO application and using the device for other purposes

The device-based applications often use hardware specific capabilities in order to fulfill the above requirements, which results in new aspects that need to be considered:

- The ePRO software can only be used on hardware platforms that support the capabilities used[1,3]
- Every release of the device-based application needs to be validated with every release of the hardware it is used on to ensure that the software operates as required (e.g., the user is still blocked from deleting data on the device)[1,3]

PRO instruments and requirements

A PRO instrument is the collection of questions and scales used to elicit information from the subject. It is not dependent on technology as such—a PRO instrument can be implemented on paper, using an ePRO solution or both. However, there is a regulatory requirement that the PRO instrument be shown to measure the correct information to support later uses of the PRO data, for example, in labeling claims. Typically this is shown by validating the PRO instrument.[1,3,4]

One concern has been that a PRO instrument that has been validated in one implementation (usually on paper) may not produce the same results if it is transferred to a new medium (such as ePRO). The concern has been that differences in layout, the presentation of the question, the number of questions presented at the same time, and the size of scales and other similar aspects could influence patient responses. One large study (looking at 46 trials and 278 scales) was carried out to investigate these concerns.[5] The conclusions reached were that the responses collected from the subjects were comparable even when using different media (paper, ePRO). Other similar studies[6,7] have shown that minor changes caused by changing from one media or device to another did not adversely affect the results, but larger variations in the presentation, such as rewording or reordering the instrument, could result in the results not being comparable.

New technology

We now have a potential pool of subjects for clinical trials to whom the use of web-based software and mobile computing platforms is commonplace. Web-based applications are now to be found in most users' Internet histories—buying goods and services online, social media, and personal banking are web-based services now used by most of us.

Connectivity and computing power are areas that have seen a dramatic development and evolution in the last five to 10 years. Smartphones and tablet computers that are more powerful than the desktop computers used just a few years ago are gaining market share. According to reports from Gartner[8] and Statista,[9] worldwide smartphone sales in 2012 amounted to a little more than 722 million units, of a total 1.746 billion mobile phones sold. In 2013, smartphones were projected to account for 958 million of a total of 1.8 billion mobile phones sold. In addition, by 2015, tablet computer sales were estimated to reach 325 million, while PC sales continue to decline (see Figure 1).

As these trends show, more subjects recruited for clinical trials will have advanced mobile computing platforms, platforms that are more advanced than today's ePRO devices. The standardized delivery of software installed on the client platform (computer, smartphone, or tablet) has also been revolutionized by the use of apps, which are now even used to install software on other consumer products such as Smart TVs. This enables the easy delivery (over the Internet) and installation of proprietary software on the consumer's own device.

App or web-based application?

What are the advantages and disadvantages of the two new technology solutions that offer us the possibility of using the patient's own device—web-based applications and apps?

Validation

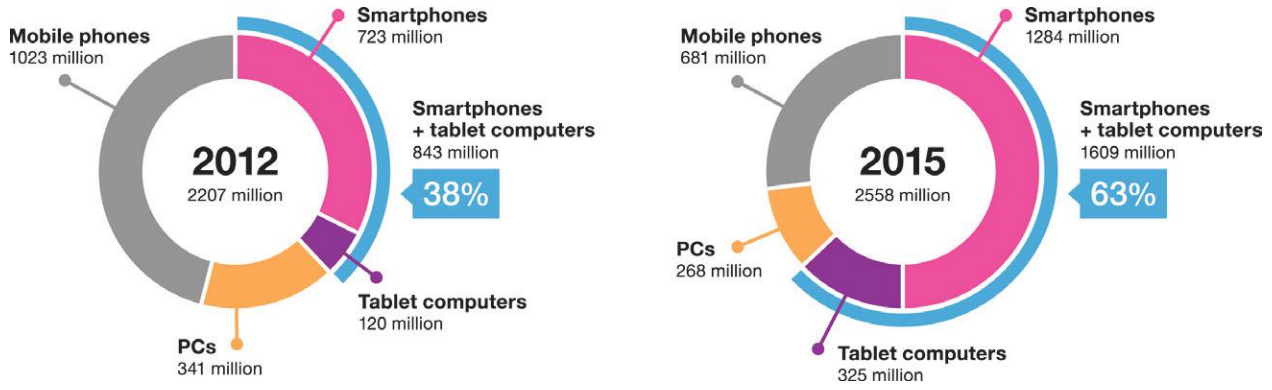
A web-based application requires validation for every supported combination of operating system (i.e., iOS, Android, Windows) and browser (i.e., Safari, Chrome, Explorer, etc.). There is little or no requirement for device-specific validation.

When using apps, there are still some differences between platforms and devices. The user does not have to look far to find examples of apps that run on some phones and tablets but not on others.[10] Hence, the introduction of the app methodology has helped standardize the software environment, but the basic validation requirement is still the same—the instrument must be validated on every type of mobile phone, tablet, and computer used in the trial.

Offline

The greatest single disadvantage of a web-based application is that you must have Internet connectivity in order to

Worldwide Mobile Platform Market Shares



Source: Yeomans, December 2014.

Figure 1. *Comparing worldwide mobile platform market shares in* 2012 *versus estimates for* 2015.

use it. The latest HTML standard (HTML 5) has introduced limited offline capabilities, but you still need an Internet connection to submit and store the data once the questionnaire has been completed.

The use of a local app allows for local storage of data and synchronization with a central database at a later time when connectivity is re-established. This is a well-established method used by existing legacy solutions and accepted by the regulatory authorities. The only major risk (which is the same for existing legacy solutions) is the risk of losing data if the device is lost or if it should break down.

Installation

A web-based application has a zero footprint on the patient device and no need for local installation on the patient device.

A local app does require installation, and although modern systems (iOS, Android, and Windows) have simplified the downloading and installation of apps, it still must be done. And this also brings into play a range of requirements mentioned earlier regarding device-based applications:

- The need to prevent patients from modifying the app or the data stored on the device
- The need to prevent patients from installing and using other apps that may influence the ePRO app or the data collected.
- The need to prevent patients from deleting the ePRO app

A web-based application simplifies the use of ePRO instruments in all cases except when an offline capability is of vital importance to the trial. Although the use of an app simplifies the distribution and installation of software and can help ensure that the ePRO instrument looks the same on all supported devices, it does not address the other issues facing the legacy device-based applications, as an app is after all still basically a device-based application.

The use of app technology is an improvement on the existing legacy device-based applications, but it is not a radically new idea—it is simply a standardized environment for the distribution of, installation of, and the operating system for computer software. It is a step toward the future in software development in general that started with the use of Linux (which also delivers all three of those benefits, although the use of Linux is limited for mobile computing platforms).

The future of ePRO platforms can be even brighter when considering web-based applications.

The issues

We want to collect PROs in a fashion that ensures the data collected is correct, dependable, and repeatable, in terms of both:

- Producing comparable responses from the same subject over time
- Producing data that is comparable between subjects

There are a number of challenges to be faced if we want to use the possibilities presented to us by the spread of smartphones and tablet computers.

One of the most important issues is that of validation of the PRO instrument. Attempts to use the subject's own mobile phone for ePRO have often been rejected due to problems with validation of the PRO instrument. The arguments used include:

- How does the sponsor show that the data collected supports their claims, when subjects are using different devices, with different sized screens and varying graphical interfaces?
- How can they ensure that the results are comparable except through validation of the instrument on every type of mobile phone used in the trial?

The cost of such a validation effort is prohibitive.

The solution

The studies mentioned earlier[5,6,7] give a clue to how such a situation can be handled. Their findings indicated that minor changes in appearance of the PRO instrument still produced comparable results. This can be leveraged by ensuring that:

1. Devices with comparable capabilities are used. Smart phones and mini-tablets all have similar sized screens, similar graphic resolutions, and similar colors.

2. The PRO instrument needs to utilize a common graphical denominator that appears the same on all devices (e.g., all answer choices are shown without scrolling). When using larger tablet computers and PCs, then the same limited area should be used for display as on smart phones and mini-tablets.

3. The use of a single application across all devices ensures the same "look-and-feel" within the PRO instrument with regards to ordering and presentation.

4. The use of a web-based application would mean there was no software installation required on the subject device.

5. The use of a web-based application counteracts the need for computer system validation on each possible platform.

The study protocol and the design of the PRO instrument should take into account the need for comparability in responses across slightly different devices, and, thus, avoid cases that could potentially create difficulties. The use of advanced graphical scales, such as graphical body representations (e.g., point at the part of your body that is in pain) is generally considered to be more dependent on exact equivalence in the graphical representation than textual questions and answers. To ensure compliance across multiple devices, the body could be divided up into different areas (head, shoulder, etc.) that are highlighted if the subject clicks on any part of that area.

How many of the prospective subjects in our clinical trials have their own smartphones? Market analysts predicted[11,12] that the major pharmaceutical markets will pass 50% market penetration for smartphones from 2012 to 2014. If a subject group contains subjects that do not own a device suitable for use in the trial, then a mixed model can be used. The advantage of a "subject's own device" model is that it implicitly allows for varying devices to be used in the same trial. One advantage is that even if a subject changes device in mid-trial (e.g., purchases a new smartphone), then data compliance is still maintained.

Regulatory aspects

It is absolutely essential that any system used to collect data for clinical research is compliant with the regulations and guidelines covering this work. So when evaluating the use of new technology, it is especially important to highlight the areas that differ from existing solutions, and whether these areas require special consideration in order to ensure regulatory compliance.

The use of a web-based software application instead of a device-based application does not alter the fact that the software used needs to be documented and validated in exactly the same way as all software in the industry is handled. It is also the responsibility of the investigator and trial sponsor to formally document a risk assessment (Quality Risk Management Plan) for the continuity of data entry when a subject loses his or her device or decides to get a new one. This already applies even when using legacy device-based applications, hence, there are no extra burdens when moving to a solution based on the patient's own mobile computing platform.

When using a legacy device-based application, it is vital that the user cannot influence either the application or the data stored locally. An important functionality (and validation step) to be considered when developing device-based applications is how to disable user access to the software and data, and validating that there is no way the user can get at the software or data.

The following problems when using device-based applications are automatically solved by the use of a web-based application:

- Loss of data due to loss of device or device malfunction
- Collection of incorrect data due to the latest protocol amendment not being implemented on the device

The solution of these issues for device-based applications involves additional software, and, therefore, additional validation effort and additional risk.

Using the patient's own mobile computing platform provides substantial savings from a regulatory compliance point of view. There is no software installed on the remote device, nor is any data stored. Therefore, the fact that the patient's own device is being used becomes almost unimportant—as long as it supports the web-based application, no further validation is required. Platform support can be programmed into the web-based application itself in the form of requiring certain versions of given browsers; if they are available on the patient's device, then there is no problem. The use of the patient's own device then becomes directly analogous to the use of a telephone in an IVRS system—there are no requirements to validate IVRS systems against all possible telephones in all countries in the world; it is enough that standard telephone functionality is available to the subject.

Summary

What are the advantages that a subject's own device solution offers? The major advantages were named in the opening paragraph, namely provisioning, supply, training, and maintenance. When would the legacy IVRS and device-based applications be more suitable? IVRS solutions do not require a mobile computing platform; they operate on any telephone. In this respect, they are still applicable for all potential subjects that have access to a telephone, but not to a smartphone, tablet computer, or PC. This is currently a large, but diminish-

ing, proportion of the overall pool of subjects. Device-based applications can still be the solution of choice for trials with specific requirements for a uniform hardware solution. One example is a requirement to connect to external equipment at the subject's residence, such as PEF meters and blood pressure cuffs.

The future is already here

It would appear that there are few, if any, insurmountable problems with the use of the subject's own device. If the study protocol and the PRO instrument have been designed with this in mind, then the ePRO comparative studies already conducted[1,6,7] indicate that the subject's own device can be used.

Traditionally, large corporations in the clinical research sector exhibit a certain resistance to adopting new technologies, but are there any regulatory or other substantial concerns that would contraindicate adopting the patient's own mobile computing platform for ePRO? As can be seen from the previous summary, the answer is no.

So why isn't this already being done? Actually, it is—all around the world, trials are presently being run that collect ePRO data in this fashion, including studies critical to regulatory submissions. The FDA[1] and the European Medicines Agency (EMA)[4] have issued guidelines and reflection papers, which outline their current thinking when it comes to compliant use of ePRO.

Examples of studies using a web-based application on the patient's own mobile computing platform include:

A Phase II clinical trial in the U.S. testing the use of a new pharmaceutical designed to increase sexual desire, arousal, and satisfaction in females with sexual desire disorder. The ePRO data contains primary efficacy data as the measure of success of the treatment and is heavily dependent on the qualitative responses from the subjects. The trial included more than 200 subjects at more than 15 sites in the U.S.

A medical device trial in Europe to evaluate an additive for pain relief in a plastic surgery product used for cheek shaping. Again, the ePRO data containing primary efficacy data as the measure of the degree of pain relief is heavily dependent on the qualitative responses from the subjects. The trial included more than 50 patients at three sites.

An investigator-initiated Phase IV trial in Japan to test the efficacy and safety of three types of hyaluronic acid injections into patients with osteoarthritis of the knee. The ePRO data collected is a quality of life questionnaire containing the WOMAC scale. The trial included more than 600 patients at 30 sites.

If the design of the study protocol and the PRO instrument aims at being comparable across different devices, and the study population is chosen such that the subject's own device can be used for data collection, then clinicians can run one of the new breed of ePRO trials already out there.

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References

1. U.S. Department of Health and Human Services. "Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims." December 2009.
2. Vendors of e-PRO device-based solutions: PHT Corporation—http://www.phtcorp.com [4], eResearch Technology (incorporating Invivo Data and Clinitrac)—http://www.ert.com/CRF [5] Health—http://crfhealth.com [6]
3. European Commission Health and Consumers Directorate-General. Annex 11: Computerised Systems from EudraLex, "The Rules Governing Medicinal Products in the European Union," Volume 4 Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use
4. EMA Committee for Medicinal Products for Human Use. Reflection paper on the regulatory guidance for the use of health-related quality of life (HRQL) measures in the evaluation of medicinal products; EMEA/CHMP/EWP/139391/2004
5. Gwaltney CJ, Shields AL, Shiffman S. "Equivalence of Electronic and Paper-and-Pencil Administration of Patient-Reported Outcome Measures: A Meta-analytic Review." Value Health 2008;11:322-33.
6. Coons SJ, Gwaltney CJ, Hays RD, et al. "ISPOR ePRO Task Force Recommendations on Evidence Needed to Support Measurement Equivalence Between Electronic and Paper-based Patient-reported Outcome (PRO) Measures: ISPOR ePRO Good Research Practices Task Force Report." Value Health 2009; 12:419-29.
7. Juniper EF, Langlands JM, Juniper BA. "Patients May Respond Differently to Paper and Electronic Versions of the Same Questionnaires. Respir Med 2009;103:932-4.
8. Gartner: Gartner Says Worldwide Traditional PC, Tablet, Ultramobile and Mobile Phone Shipments On Pace to Grow 7.6 Percent in 2014, http://www.gartner.com/newsroom/id/2645115 [7]
9. Statista: Global smartphone shipments from 2010 to 2017 (in million units), http://www.statista.com/statistics/263441/global-smartphone-shipments-forecast/ [8]
10. "Fitbit" is an example of a common App available for both iOS and Android that does not support all devices on either platform, see: http://www.fitbit.com/uk/devices [9]
11. Nielsen: Mobile Majority U.S. Smartphone Ownership Tops 60%, http://www.nielsen.com/us/en/newswire/2013/mobile-majority--u-s--smartphone-ownership-tops-60-.html [10]
12. eMarketer: Smartphone Adoption Tips Past 50% in Major Markets Worldwide, http://www.emarketer.com/Article/Smartphone-Adoption-Tips-Past-50-Major-Markets-Worldwide/1009923#BDPmZj33rlE8fTVX.99 [11]

Driving Change Through eCOA Innovation

James Munz

ERT's Innovation Lab explores possible technology uses in clinical trials with minimal risk exposure.

Pharmaceutical research is being driven toward change through many channels. Global regulators are promoting electronic data capture as the preferred clinical approach, payers are recommending patient-centric healthcare to improve quality of life while expanding availability of services, and patients are demanding greater access to individual health monitoring devices in order to be more responsive to health changes in near real-time. Pharmaceutical companies have responded to these drivers in many ways–one of which is the widespread adoption of electronic devices like smartphones and tablets for capturing electronic clinical outcome assessment (eCOA) data in pivotal clinical trials. The benefits of eCOA have been repeatedly proven with improved patient protocol compliance, greater study power and regulatory acceptance. As a result, the use of patient electronic diaries (eDiaries) has seen significant uptake; 73% of clinical trials are expected to include the use of eCOA in the next two years[1].

Concurrently, the development of new medical devices with wireless integration capabilities is increasing. Once approved by the FDA, the integration of eCOA and these devices could potentially offer significant improvements in efficiency and accuracy during new drug research and development.

This evolution is driving changes within pharmaceutical research. The question remains–how quickly can the potential for improved patient participation and better data be adopted?

A world of wearables and mobile solutions

It's difficult to discuss the future of healthcare without mentioning mobile health solutions and wearable devices. Advancements in these technologies are changing paradigms in pharmaceutical research with the promise of significant improvements in subject recruitment and engagement, data management and operational efficiencies. Transformative trends in the industry are conducive to remarkable growth in mobile applications–population aging, increasing chronic illness, accelerating health costs, new regulatory reforms and increased consumer demand for health information and self-care will drive mobile solution growth[2]. Consumer demand across all age groups for real-time self-monitoring of personal health information and technology are driving a surge in the development of new healthcare solutions.

A number of technology giants have recently entered the healthcare market with apps, portals and bio-wearables for personal use. The Apple ResearchKit® recruited thousands of subjects for clinical trials within months of launch; the Microsoft HealthVault® includes over 250 medical devices for data collection and safe storage in the cloud; and Google is partnering on medical devices such as continuous glucose monitors and funding development of a watch for use in the clinical environment. Such significant investment by leading technologists is evidence of the surging market for personal healthcare. Whether they can also tap into clinical research will be the global regulators' decision as consumer devices must

satisfy FDA guidelines as a medical device before used within a clinical trial.

The emerging global market for wearable technologies is expected to reach $30 billion in revenue by 2018[3]. As existing healthcare technologies mature and as new products enter the market, the possibilities for their use in pharmaceutical research appears endless. There is no limit to how these technologies can be leveraged to gain complete insight into the patient experience by integrating varied, multiple data streams with eCOA data collected during clinical trials. With all of this in mind, how can industry leaders choose from the myriad devices and technologies, manage the endless amount of data, as well as mitigate potential risk of the technology use within the evolution of the clinical trial?

Reducing risk while exploring possibilities

ERT–a provider of eClinical trial and healthcare solutions–has been integrating medical devices within its eCOA system since 2005. Peak expiratory flow (PEF) meters, glucometers, cardiac holters, wireless electrocardiograms (ECG) and activity meters have been successfully integrated and deployed in global clinical trials, helping sponsors collect subjective and objective data for a more complete view of the patient experience. As a result, industry researchers frequently request ERT eCOA scientists, regulatory and technological experts to evaluate consumer and FDA-approved devices for integration, patient preferences and usability testing.

To accommodate this surging demand from pharma and medical device manufacturers, ERT has built an innovation practice that facilitates the development of concepts to enhance data collected from patients. The ERT Innovation Lab is home to diverse technologies re-purposed for clinical research and broad clinical care. Its objective is to reduce risk while expanding the art of the possible for research.

ERT eCOA clinical scientists, engineers, usability experts and specialty resources, such as telecommunications experts, are teamed up to achieve each projects' goals. Each project gains access to leading technologies for use within clinical trials, while ensuring safe market testing prior to use. The ERT Innovation Model is based on lean development philosophies with results returned within days and weeks, not months.

Although the physical Lab facility will officially open this fall within ERT's Boston office, customers and partners have already begun leveraging the Innovation Lab resources. One project integrates biometric data captured via an FDA-approved wearable biosensor patch into the ERT eCOA system. The patch captures and wirelessly transmits real-time, continuous, clinical-grade measurements of ECG, respiratory rate, heart rate variability, skin temperature, physical activity, posture, and fall detection. As a proof of concept, ERT is capturing patient fall detection data from the patch biosensor and using it to trigger an episodic eDiary assessment to capture information about the circumstance of the fall. As clinical trials are identified for appropriate use of this technology, trial sponsors will be able to capture and integrate one or more of the vital statistics with patient-provided eCOA data to support clinical benefit.

Successful innovation

Historically, investments in internal innovation labs have proven risky, often marked by low adoption rates for explored concepts. Some models are unsustainable; they consume too many resources and have long time windows without demonstrating value through project use, providing feedback to mature a concept, or determining that a concept is not fit for purpose. Many innovation efforts fail because the directive is to keep innovations under the radar to protect the concepts they are working on for future IP development, thus stifling valuable collaboration.

To address those challenges, the ERT Innovation Lab focuses on projects that are time boxed allowing for targeted commitments from all parties interested in the problem statement being worked on and keeping budget requirements manageable. Collaboration partners may provide funds and resources toward the problem being worked on, and share all lessons learned at the end of the project cycle. Innovation projects include initiatives in the Internet of Things, consumer medical device assessments, data analytics, new-age hardware components and process improvements for logistics, recruitment and trial management.

Having a dedicated team in the Lab allows for more collaborative opportunities, including:

- Innovation Days, onsite and remote tours for partners
- Working sessions to review "Innovation Roadmaps" and provide feedback based on the collective teams' experience and identify partnership opportunities
- Innovation sessions enable a collaborative and safe environment to try ideas against the potential impact on the clinical trial, along with realistic adoption timelines

By enabling industry to leverage the Lab with minimal risk and rapid deployment, ERT has enabled researchers to embrace new medical technologies and think more broadly about how to evaluate the complete patient experience during clinical development.

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References

1. ISR Report, 'EDC and ePRO Market Dynamics & Service Provider Performance Report', 2015
2. mHealth in an mWorld: How Mobile Technology is Transforming Health Care, 2012 Deloitte Development LLC https://www2.deloitte.com/content/dam/Deloitte/us/Documents/life-sciences-health-care/us-lhsc-mhealth-in-an-mworld-103014.pdf.
3. IHS Technology Intelligence Service, Wearable Technology: Primary Source and Forecast Data on Wearable Technology

Is a Bring Your Own Device the Best Approach to eCOA?

Paul O'Donohoe

Because of challenges associated with BYOD, it may not always fit your trial needs.

As smartphones become ever more omnipresent, and consumers become increasingly tech-savvy, the industry has reached a point when it can finally begin to consider harnessing the low-friction, rich, real-time data that can be captured using patients' own devices. The bring-your-own-device (BYOD) model holds the promise of bringing an array of benefits to clinical trials. However, to implement a BYOD methodology successfully, certain requirements and criteria need to be met. Rather than a one-size-fits-all model, sponsors and CROs must weigh the benefits of the approach against the needs of their unique protocol. Here we discuss the factors that should be considered when approaching a BYOD design for electronic Clinical Outcome Assessments (eCOA) and provide insight into why certain barriers mean the model might not always be the most appropriate.

Real-world rationale

Traditionally in clinical development, patient data has been captured via provisioned devices (i.e. providing all participants within a study a device on which to provide data), however, the last couple of years has seen a remarkable rise in the number of sponsors and CROs looking to design their clinical trials around a BYOD strategy. However, not restricted to just the continue growth of smartphones, BYOD can allow clinical trial subjects to use tablets, laptops and desktop PCs to access and respond to study-related patient reported outcome (PRO) assessments.

The shift toward BYOD is much anticipated by sponsors and promises a transformation of how field-based electronic patient reported outcome (ePRO) assessments are implemented in clinical trials. Its use offers multiple advantages. For patients, allowing them to use their own device retains optimal familiarity and reduces the perceived burden of having to carry around an additional device for the duration of the study. It also means that the trial can fit into their everyday schedule, improving accessibility and usability, and making it simpler to meet study obligations. Coupled together, these factors improve the patient's overall experience, which should have an associated positive impact on compliance and data quality.

For sponsors, a BYOD approach has obvious advantages. By eliminating the need to source and provision dedicated handheld devices to the entire patient population (not to mention maintaining, shipping and distributing to sites/subjects), sponsors can save vital time and funds. On a similar note, by eliminating the need to store devices, as well as receive deliveries and return devices etc., sponsors and CROs can significantly reduce the burden on study sites.

Regulatory viewpoint

In terms of regulatory stipulations on how a BYOD methodology should be implemented, there is currently no official guidance from the regulatory bodies around BYOD trials. Subsequently, a major concern for sponsors and CROs is whether the data captured as evidence will be accepted by the

regulatory bodies. The scientific guidelines for the development, administration and interpretation of PRO instruments are included in regulatory guidance from the FDA and EMA[1,2]. Although these don't address BYOD issues directly, they include some fundamental principles that must be considered when implementing a BYOD trial design.

As with any regulatory submission, data consistency, quality, integrity, attribution and proof of the chain of custody all need to be transparent. To provide further guidance on this, the ePRO Consortium, which was established by the Critical Path Institute to advance the quality, practicality and acceptability of ePRO data capture methods used in clinical trials, offers further support on best practice approaches.[3]

Challenges and considerations

Despite clear benefits and a promising outlook for BYOD clinical trials, there are a number of important considerations for sponsors and CROs when it comes to opting for this approach. Firstly, although smartphone penetration is increasing, not everyone owns one and, therefore, organizations need to ensure study enrollment is not biased by technology ownership, age, socioeconomic status, etc. Any bias driven by smartphone ownership would be frowned upon by regulators, so suitable planning to allow patients without a device to partake in studies would need to be made. To address this, sponsors and CROs could consider implementing a hybrid approach, where patients who own smartphones enter their data using the app on their own device, and those who don't are provided with a dedicated device. That said, while this approach would address any bias issues, it could reduce the hoped-for cost benefits of a BYOD methodology.

To reduce bias further and ensure the trial is accessible to as many patients as possible, make sure your app works across the most widely used operating systems (Android, iOS etc) or web browsers (Internet Explorer, Chrome etc).

Another key outstanding question is the issue of equivalence and the comparability of data captured across the wide range of devices that could potentially be involved in a BYOD trial. For example, someone using a home-based desktop computer may be limited as to when they can make entries, whereas someone using a smartphone can respond at any time. It is also likely that these different modalities will have varying screen sizes, which might influence how patients interact with them. Regulators have raised concerns this has the potential to impact data integrity. Although it should be noted that the large amount of work done comparing paper to EDC modes suggests this is not a significant concern.[4,5]

Some have also raised concerns over data security. There is a belief that provisioned devices are inherently more secure than personal devices. However, strong encryption ensures the security of patient data, whether it's delivered through a personal or provisioned device.

The costs associated with data transmission when subjects use an app-based solution also need to be considered. In studies where devices are provisioned, the device SIM controls data transmission, with the sponsor meeting the costs. In a BYOD model, it has to be clear how reimbursement will be managed. Problems could be encountered with subjects who do not want to be responsible for additional charges incurred due to reimbursement rates or timelines, or if patients use up their data allowance during a given period.

Finally, by allowing the patient to use their own device, sponsors and CROs have to relinquish some control. For example, sponsors cannot force the participant to have notifications turned on, or unmute phones for audible alarms, which could potentially lead to compliance issues. Also, patients could delete the app, thus losing any unsubmitted data.

There are real arguments to be made that BYOD could eventually replace significant elements of eCOA. However, for the time being, the above challenges remain very real issues. While the industry is currently thinking of ways to address each of these, for the moment the design of hybrid BYOD studies offers an ideal starting point and presents a half-way house for sponsors and CROs taking their first tentative steps into the approach.

Where are we now

While it could be that BYOD does offer higher compliance, provisioned eCOA studies already see compliance of higher than 90%. In many ways, technology has outpaced our understanding of how BYOD can best function in clinical trials, so the industry now needs to gather empirical evidence that will allow for more general conclusions on how BYOD can be applied in clinical trials.

Although there is no doubt that BYOD will transform clinical research and patient experiences in the future, flexible solutions will always be necessary to provide different options for patient-driven data streams.

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References

1. EMA. Reflection Paper on the Regulatory Guidance for the Use of Health Related Quality of Life (HRQL) Measures in the Evaluation of Medicinal Products. Londo. 2005.
2. FDA Guidance for Industry Electronic Source Data in Clinical Investigations. 2013.
3. http://c-path.org/programs/epro/
4. Equivalence of Electronic and Paper-and-Pencil Administration of Patient-Reported Outcome Measures:A Meta-Analytic Review Chad J. Gwaltney, PhD, Alan L. Shields, PhD, Saul Shiffman, PhD
5. Equivalence of Electronic and Paper Administration of Patient Reported Outcome Measures: A Systematic Review and Meta-Analysis. Muehlhausen W, Wild D, Doll H, O'Donohoe P, ISPOR 2014

PRO Use in Real-World Drug Evaluation

Chitra Lele, PhD

Measurement and analysis of patient reported outcomes to provide the patient voice.

Today there is heightened awareness among healthcare professionals (HCPs), consumers, payers and regulatory authorities on the benefits and risks of products, with all interested parties demanding more evidence than safety and efficacy data from clinical trials. Once a product is in the market, other important measurements include treatment effectiveness and comparative effectiveness relative to other therapies. These require real-world data, such as Patient Reported Outcomes (PROs) that are based on longer follow-up and a more representative sample of the patient population.

PROs and other similar tools are used to capture Quality of Life (QoL) data along the range of clinical development, post-approval studies and patient registries, which are more compelling than for example, survival or even progression-free survival data. QoL data rose into prominence a number of years back with the increase in incidence of oncology indications, high drug prices and small incremental gains in survival rates offered by the new drugs. QoL data is also equally relevant for lifestyle diseases such as diabetes and asthma. The fundamental premise now is that health-related QoL and well-being of patients is a core co-primary endpoint in clinical research and clinical care.

Many companies use PRO data to measure the impact and effectiveness of their drugs even during Phase II and Phase III clinical trials. In fact, some companies are using PROs at the very start of the drug development process[1]. Early observational and epidemiology studies can identify unmet clinical needs and potential profitable drug markets

Better decision-making

End results of medical treatment and care are available from outcomes research studies, in terms of the effect on health and well being of patients and the populations. The area of outcomes research encompasses studies that evaluate effectiveness of treatments, development and use of tools to measure health status and analysis and dissemination of the results. Outcomes research evaluates the results of healthcare process in the real world through effectiveness research rather than using efficacy studies, and assesses which treatments for specific problems work best for whom by also factoring in patient preferences and patient satisfaction. Governments, insurance companies, employers and consumers look to outcomes research data for better decision-making.

Regulators are making approval decisions based on outcomes data. For example, when NICE (National Institute for Health and Care Excellence) reviewed Novartis' asthma drug Xolair, it considered data from the Asthma QoL questionnaire in observational studies and overturned an earlier decision to reject Xolair[2]. PRO health surveys have also been used for label claims (e.g., Humira, Allegra, Lyrica)[3]. PRO data can help influence pharmacy benefit managers and insurers to include a drug in their formularies. Health surveys can also be used to answer any questions regarding comparative effectiveness in order to build an economic basis

The evaluation of a PRO instrument includes the following considerations:
• The population enrolled in the clinical trial
• The clinical trial objectives and design
• The PRO instrument conceptual framework
• The PRO instrument measurement properties

PRO instruments' measurement properties included in the review are:
• Reliability (intra- and inter-interviewer reliability, internal consistency)
• Validity (content validity and construct validity)
• Ability to detect change

for formulary inclusion, thus helping to lower claim costs over time. Companies successfully use PROs to prove the positive impact of a product on patient health and ultimately health expenses.

Public and private sector interest in outcomes research has grown dramatically in the past several years, in large part because of its potential to address the interrelated issues of cost and quality of healthcare. Outcomes research touches all aspects of healthcare delivery, from the clinical encounter itself to aspects of the organization, financing and regulation of the health care system. Each of these factors plays a role in the outcome of care, or the ultimate health status of the patient. Understanding how the different factors interact requires collaboration among a broad range of health services researchers, such as physicians and nurses, economists, sociologists, political scientists, operations researchers, biostatisticians and epidemiologists.

Standardizing patient perspectives

The primary challenges of real-world data are that these data are not controlled, they may be collected and measured anywhere. The main sources are computerized databases, EHRs and PROs. The PRO data measure health status and consumer preferences and capture the patient perspective of the impact of intervention on quality of life and ability to function. It is a challenge to quantify and calibrate these data. Collection of such data requires tools (PRO instruments) that provide scientifically valid assessments of physical and mental health, to measure health and well-being from the patient point of view. There are a few tools that offer a standardized way to measure health outcomes for individuals and large populations, as statistically valid patient-centred measures. Health status is measured as physical functional status, role functioning, social functioning, physical and mental well-being, measured in terms of mental health (mood, depression, anxiety), health perceptions (own view of general health), pain and life satisfaction (QoL), all of which require an individual evaluation[4].

In December 2009, the US FDA released guidance for the industry on PRO measures[5]. This guidance reviews and evaluates PRO instruments used to support claims in approved medical product labelling. A PRO instrument (such as a questionnaire plus the information and documentation that support its use) is defined as a means to capture PRO data used to measure treatment benefit or risk of medical products.

The adequacy of any PRO instrument, as a measure to support medical product labelling claims, depends on whether its characteristics, conceptual framework, content validity, and other measurement properties are satisfactory. The FDA will review documentation of PRO instrument development and testing in conjunction with clinical trial results to determine whether a labelling claim is substantiated. The type of PRO information sponsors should provide to the FDA to facilitate instrument review is listed in the guidance document.

The use of electronic PRO instruments, however, may pose a problem when direct control over source data has to be maintained by the sponsor or the CRO and not by the clinical investigator. Sponsors need to plan to establish appropriate system and security controls, as well as cyber-security and system maintenance plans that address how to ensure data integrity during network attacks and software updates. Capture of PROs may also be web-based or through IVR-compatible tools.

A commonly used PRO instrument to measure functional health status is the Short Form (SF) Health Survey (SF-36v2® Health Survey of 36 questions and the shorter SF-12v2® Health Survey of 12 questions). This measures health status across eight domains and are summarized into physical and mental health scores.

Statistical complexities

Variables defined from PROs may be the main variables that will be analyzed to yield the key conclusion from the study, or they may be add-on variables while the main variables may be based on clinical data. In either case, when PRO data are collected, it becomes difficult to identify a single variable as the most important. Therefore, two or more variables have to be considered equally important while making inferences from the statistical analysis so, multiple comparisons have to be carried out. Appropriate statistical methods have to be applied to handle this multiplicity and adjustments need to be made to control the overall rate of false positives. Adherence to blinding and randomization requirements is critical in order for the analysis of the PRO endpoints to be valid since the patient reported outcomes are inherently subjective in nature.

A PRO instrument (tool or questionnaire used to capture PRO data) comprises of multiple domains (e.g., physical and mental, social and work-related), some of which may be combined to define the variables on which the statistical methods are applied. Analysis of such variables and interpretation of the results is challenging, especially when a conclusion has to be made on individual components of the variable. PRO

data are often measured at regular intervals over a period of time and statistical models have to factor in the dependency in the data since it's measured on the same individuals at different time points. When outcomes have to be captured over a period of time, the possibility of some data being missing is quite high and this could lead to bias in the results. Sensitivity analysis has to be carried out by replacing missing data with substitute values. Since the PROs measure well-being of patients, cross-cultural comparability of data can be a major issue even when validated translated versions of the PRO instrument are used.

Thus, the analysis of PRO data involves substantial statistical complexities. Moreover, clinical interpretation of results and assessment of clinical significance can also be very challenging. It is important to use the right skills to design, analyze and report PRO endpoints. Outcomes research is often a specialized and separate group within the R&D or commercial organizations of pharmaceutical companies. There is increased recognition that PRO data, even when it is collected in the post-approval phase, is challenging to capture, analyze, interpret and report. With the increasing volume of outcomes research data, sponsor organizations often need to outsource some of the analysis. Many CROs and other niche providers have been building expertise in handling PRO data to cater to this need. Outsourcing to the right provider will give an edge to the sponsor organization in this increasingly important and complex area of data analysis and reporting.

Benefits of PRO

PRO health surveys generate information that is tailor-made for the marketing of a product. Consumers want to know what a drug does and how well it works. PRO results can be used to convey the value of a drug and encourage patients to ask their doctor about a drug. Marketing professionals can use PRO data to create well-defined marketing communications such as advertising, brochures and educational materials to increase brand awareness, and promote sales. Companies are also using online PRO health surveys to generate web traffic in order to engage and educate consumers. Such methods help create on-going dialogue and relationship with a large number of consumers. They educate consumers on disease and treatments, which in turn leads people to talk about the products to their doctors.

Companies try to protect the safety of consumers through post-marketing surveillance, however, once a new drug is made available outside of the controlled environment of clinical trials, it can be difficult to monitor drug response and effects. By using PRO surveys at every stage of the drug development and commercialization process, a drug company can accumulate an impressive body of data to meet the demands of all interested parties, from the FDA and health insurers, to doctors and patients. A company can also solidify its position as an industry leader by consistently finding and cultivating profitable new markets. Through innovative uses of PRO health surveys, drug developers can meet the ever growing challenges created by increased competition and regulatory requirements in a world where the trial never ends.

Summary

It has become more and more common in clinical trials to assess QoL and other PROs, as part of post-approval studies to provide the 'patient voice' in evidence on treatment effectiveness. PROs are relevant to many primary care research questions and play a significant role in drug approval and labeling decisions. Thus, it is crucial to have a robust plan for capture and analysis of PRO data, which sufficiently address all challenges of capturing reliable and validated data, as well as statistical complexities involved in analysis of the data and drawing clinically meaningful extrapolations. Both logistical and scientific issues should be addressed to ensure that the PRO data is of a high quality as PROs are often inadequately reported in trials, which limits the value of these data.

Improved reporting of PRO data will facilitate robust interpretation of the results from clinical studies and informed patient care. It is only through outsourcing these activities to a provider with rich expertise and best in class processes for handling PRO data, that scientists and clinicians will overcome the challenges associated with the time and resource required to interpret and present complex data in an effective and efficient manner.

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References

1. Peter Mansell, 2012. Pharma needs to take strategic approach to patient-reported outcomes, says report. (Internet) http://www.pharmatimes.com/Article/12-05-17/Pharma_needs_to_take_strategic_approach_to_patient-reported_outcomes_says_report.aspx#ixzz3RwaTkRkW [Accessed 12/01/2015]
2. Nick Taylor, 2014. Analyzing real-world data for Lifecycle Management. (Internet) http://www.fiercebiotech.com/offer/analyzingdata?source=listing [Accessed 12/01/2015]
3. Gus Gardner, 2009. The Trial Never Ends. (Internet) https://www.optum.com/content/dam/optum/resources/articles/TheTrialNeverEnds08.11.09.pdf [Accessed 15/12/2014]
4. Foundation for Health Services Research, 1994. HEALTH OUTCOMES RESEARCH: A PRIMER. (Internet) http://www.academyhealth.org/files/publications/healthoutcomes.pdf [Accessed 12/01/2015]
5. US FDA Guidance for Industry on PRO measures, December 2009, http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm [Accessed 12/01/2015]