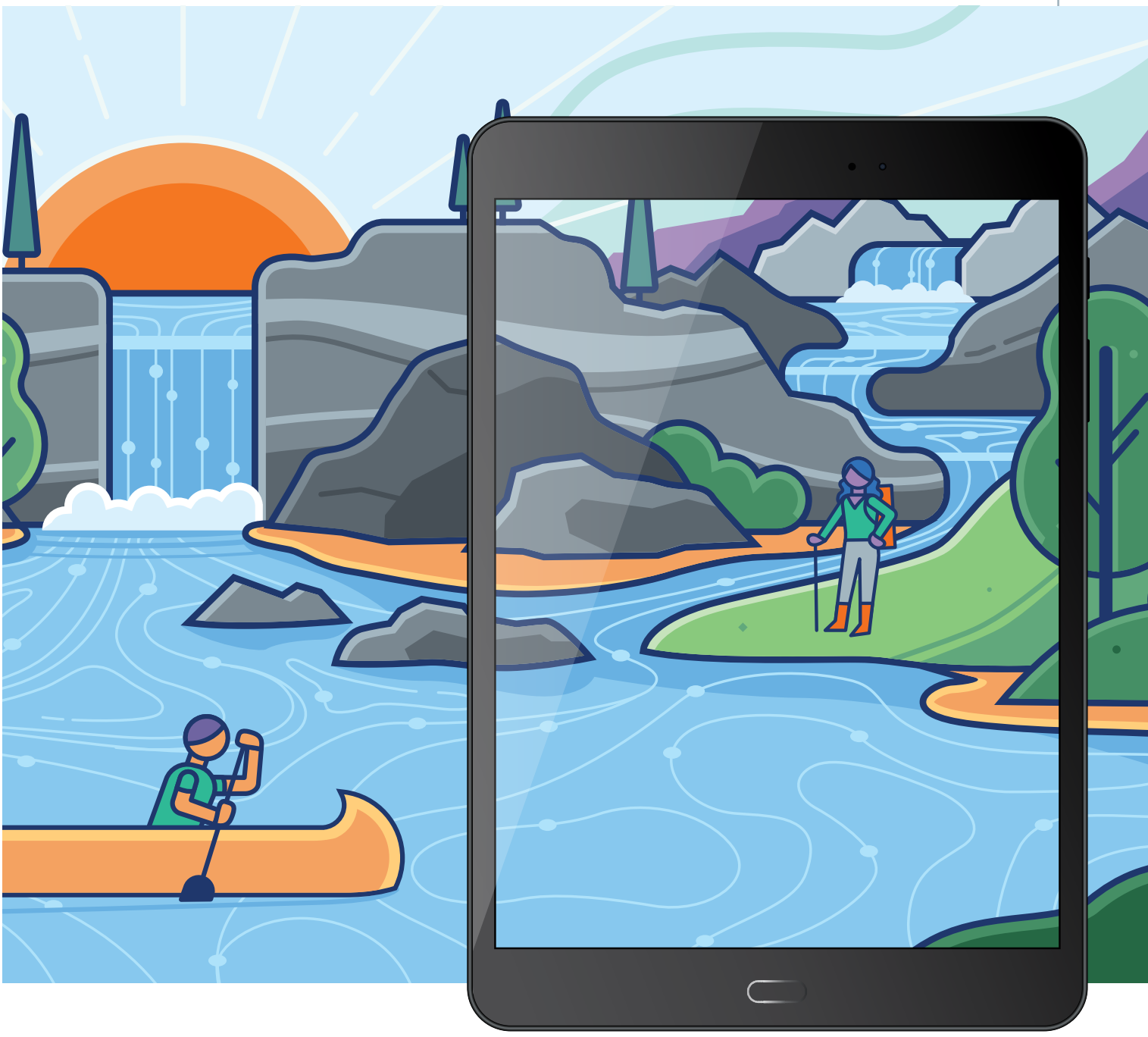
Clinical Ink®
Confident Decisions, Faster

Successful BYOD in Any Phase

By: Gena Gough
Co-Authors: Kim Romanello and Kyle Hogan

June 2019 | White Paper



Introduction

The biggest challenge facing clinical research today is the need to gather, analyze, and report data. To collect patient data more efficiently, the industry has turned to electronic patient-reported outcome (ePRO) tools, which allow patients to enter data themselves, most often on devices provided to them. With more than three-quarters of Americans owning smartphones,[1] it is only natural that researchers are increasingly exploring bring-your-own-device (BYOD) strategies for their trials; that is, allowing patients to utilize their own devices to collect data within the context of a clinical trial.

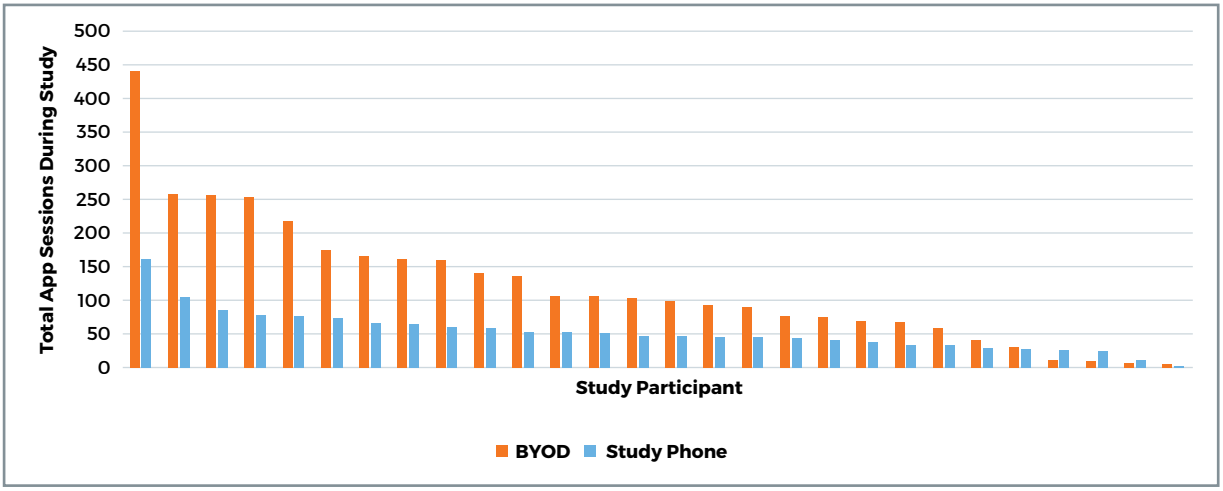
The idea of BYOD for use in clinical trials during any phase has historically been conceptualized as a futuristic alternative, rather than what it actually is — a viable option for many clinical trials. While there has typically been hesitance among sponsors and CROs to choose a BYOD model for their study, there is an increasing number of trials that have successfully deployed this model with great results. Many of the common concerns about BYOD are exacerbated by the lack of guidance on what is acceptable, as there is no official declaration by the FDA, either in favor of or against. Clinical Ink has experience with BYOD in all phases of trials, including Phase III, and their eClinical Solutions team is well-versed in the analysis that should be done before deciding whether BYOD is an option for your study.

Advantages and Misconceptions

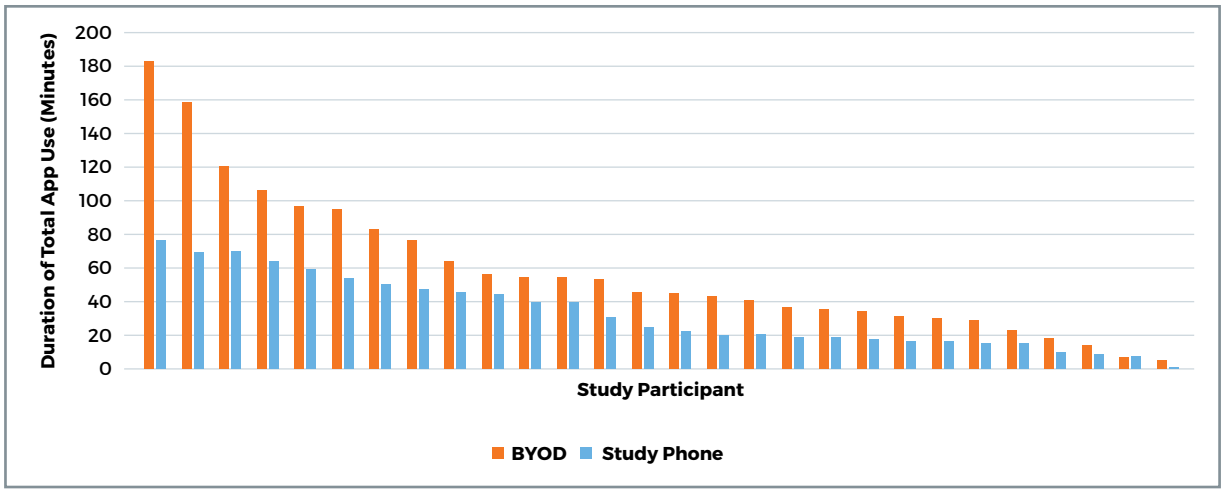
The many advantages BYOD offers make this model alluring for patients, sites, CROs, and sponsors. For patients, the convenience of using their own device is significant: no learning curve to understand a new device, no need to keep track of an extra device, and no trips to a site to pick up or return a provisioned device. And, who among smartphone users hasn't made a special trip to retrieve a cell phone that they left somewhere? While few smartphone users would be willing to part from their phones for very long, the same can't be said of provisioned devices. A forgotten, provisioned device remains just that: left behind along with a mental note to enter the necessary data later.

BYOD devices also pave the way for better compliance — BYOD patients consistently show greater use of applications provided on their own devices over provisioned devices. In an early case study conducted by Clinical Ink, patients were shown to leverage the BYOD implementation twice as often and for twice as long[2] (tables below) — which benefits sites, CROs, and sponsors. BYOD significantly lessens — and perhaps could eliminate in some trials — costs associated with data plans, shipping, lost or unreturned devices, and the overall logistics of inventory management. For a large trial, these savings could mean hundreds of thousands of dollars.

Total App Sessions During the Study (by Study Participant)



Duration of Total App Use (by Study Participant)



Despite these advantages, there remain a number of common apprehensions, driven primarily by lack of experience, fueling the industry's reluctance to embrace BYOD. Many of these misgivings revolve around patient behaviors. Researchers fear some patients may:

- Break, lose, or upgrade their phone during the trial
- Delete the app
- Change the time
- Mute or turn off notifications
- Be incapable of, for whatever reason, downloading the application
- Be unwilling to use their own data plan or storage space for the clinical trial data collection
- Not have smartphones and be unable to participate, thus creating a bias in the results

These concerns, however, often represent simple misconceptions that can be addressed either through the software or through a hybrid hardware model by simply including a percentage of provisioned devices as part of the strategy to offset the risk. The alternative, however, should not mean a 100% provisioned solution. A hybrid model allows researchers to realize the cost savings and other advantages associated with BYOD while still providing provisioned devices for patients who aren't able to use their own device, or who don't own a smartphone.

To estimate what percentage of the protocol's specific patient population will need provisioned devices requires a more in-depth look into the investigative sites' demographics. The percentage of smartphone users within the patient population must be considered, taking into account age, country, location of study, and other factors. An ePRO provider experienced with BYOD trials should be able to help with that estimate, which can be adjusted as trends emerge and the study progresses.

Importantly, patients' willingness to use their own devices appears to be strong. For example, in a recent study involving 155 patients with some form of chronic pain, 94% said they definitely or probably would be willing to download an app to their own device for use in a clinical trial. Forty-five percent indicated that their own device would be the most convenient, 15% said they preferred a provisioned device, and 40% had no preference.[3]

Some researchers believe that choosing to use BYOD might preclude sponsors from some services expected of standard ePRO vendor solutions. While this may be true from some providers, it definitely isn't universal. Clinical Ink's standard offerings, for example, do not change when implementing either full BYOD or hybrid solutions. Real-time summary reporting and diary detail continue to be available for the sponsor and CRO as do the diary design and questionnaire licensing facilitation services, patient engagement, diary reminders, visit reminders, and other standard offerings inherent to the application, regardless of the device strategy deployed.

Regulatory, Copyright, and Equivalency Considerations

To date, there have been multiple studies that have made regulatory submissions with BYOD-captured primary end point data despite the FDA being largely silent about BYOD trials. The agency's silence and absence of guidance should not be interpreted as disapproval. In fact, the FDA is willing to have conversations about BYOD on a study-by-study level. And given the agency's push to move away from paper-based trials, it is even likely that the FDA would look favorably on a trial deploying BYOD for ePRO, particularly where the alternative would be paper-based collection.

For sponsors and CROs considering BYOD, it is recommended that a range of criteria be evaluated. The priority related to these criteria will be variable depending on the specific study design and end point requirements. Below are two of the critical items which should be evaluated in every consideration:

- **Phase of trial** — as studies move from Phase I to Phase III, the degree of risk aversion related to BYOD will increase simply due to the increasing importance of the trial in the drug development life cycle. However, even in Phase III trials, there are scenarios well-suited for BYOD/hybrid strategies.
- **Nature of the end point** — as end point data being collected ranges from exploratory to primary in nature, the degree of risk aversion related to BYOD for an end point strategy will increase. However, even collection of the primary end point data for some indications and on certain validated instruments will offer scenarios well suited for BYOD/hybrid solutions.

Additionally, it will be critical to allow time to communicate with the FDA early in your protocol review to get agency feedback regarding a BYOD or hybrid strategy specific to your study population. The various questionnaires involved, the study duration, the patient population, and the role of the specific outcome measure within the trial, and more are examples of the items that you should consider and review with the FDA. BYOD and hybrid hardware solutions should be implemented as a fit-for-purpose only. Depending on the requirements of your protocol and indication, an ePRO vendor should be able to offer recommendations regarding an appropriate decision for your study.

Copyright Considerations

There has been some pushback on approval when copyrighted instruments are included in the ePRO strategy. Copyright holders of licensed, validated questionnaires painstakingly perfect their instruments before allowing them to be used. And where they have not previously evaluated their instrument for use in a BYOD setting, they may have credible reservations to be reviewed.

In the cases where copyright holders have reservations with patients using their own devices, it is critical to ensure that any approach for BYOD be reviewed and approved by them before ePRO development begins. To be sure, when implementing licensed/validated questionnaires where not approved specifically by the copyright holder, BYOD may not be a viable option. However, where copyright holders have already expressed comfort with BYOD, or the questionnaire being implemented is/has been created by the sponsor or CRO, then BYOD may be the ideal option. Discuss your specific situation with your ePRO partner. A vendor experienced with BYOD may have expertise working either with the specific copyright holder or may have an existing relationship with a representative organization such as the Mapi Research Trust, the nonprofit that manages electronic use requirements for many copyrighted questionnaires.

Measuring Equivalency

Ensuring equivalency remains a significant concern for sponsors and CROs considering ePRO trials, particularly ones using a BYOD approach. Migrating a paper-based questionnaire into an electronic format requires proof of equivalency to ensure the change in format (e.g., change in screen size, display orientation, item placement, etc.) won't affect the patient response in the measurement.

The fact of the matter, however, is that equivalency is less of a concern than it was once thought to be. Hundreds of studies and several meta-analyses have shown high levels of agreement between paper and electronic modes. Adoption is growing among copyright holders, sponsors, and CROs as more evidence becomes available about how screen size does not impact comprehension, content validity, and patient responses.

What about equivalency in BYOD specifically? The industry's first comprehensive assessment of the equivalence of BYOD compared to paper and provisioned devices was published in Value in Health.[4] This study considered if the measurement capabilities of paper-based data collection were the same as with BYOD and with a provisioned instrument. It concluded that the measurements of individual response scale types (visual analogue scale, verbal response scale, numeric response scale, etc.) were equivalent, and thus, the results are widely generalizable to the use of BYOD for a wide variety of instrument types.

Assuming that the general principles of ePRO design good practices are followed — such as those reported by Critical Path Institute's ePro Consortium[5] — BYOD is an approach that should be considered.

Getting Started With BYOD: Two Examples

As noted earlier, BYOD is not an all-or-nothing option. Sponsors and CROs wanting to experience BYOD with little risk can adopt BYOD on a limited basis. There are many ways this can be done; here are two examples.

BYOD in Screening

For studies expecting a high screen-failure rate, BYOD offers several benefits. In these cases, having patients enter their data on their own device within the screening period of the study only or throughout the entire study would either eliminate a visit to the site to return the provisioned device or require assigning a provisioned device only to patients who are successfully randomized into the trial. This makes it more convenient for the patient, saving time for the site in needless inventory management and study budget for the sponsor in unnecessary hardware costs and transmission fees.

BYOD as a Backup

For trials using provisioned devices, it may make more sense to use BYOD as the backup instead of the traditional and problematic paper backup. One immediate and significant advantage of this solution is that BYOD eliminates the need for additional, unused inventory sitting at each site just in case a provisioned device is damaged. BYOD used as a backup can drive down shipping and inventory costs for a study.

More importantly, there are other significant advantages:

- All benefits of ePRO are maintained, e.g., notifications, date/time stamps, branching logic, and edit checks
- No transcriptions or data clarification forms, thus no source data verification necessary
- Real-time data collection and monitoring are maintained, eliminating any need to email or physically deliver forms
- Modality remains constant; electronic data collection and analysis continue without disruptions
- Inventory can be reduced or eliminated; provisioned devices need be ordered only when they are required

Furthermore, this option also offers researchers a mini-pilot opportunity to explore BYOD within a specific study population. Sponsors wanting to expand on this mini-pilot could additionally make BYOD available to those patients within the study who request to use their own phones.

A BYOD Case Study

Clinical Ink recently completed a Phase III BYOD trial that resulted in exceptional compliance. In this study, allergy symptom scores were collected every 30 minutes for the first three hours on site and then every 60 minutes at home for the following nine hours on visit days, which occurred every two weeks. To enter their data, patients downloaded the Lumenis™ app on their own Android or iOS smartphone. When the patients logged into the app, they saw the symptom score rating, the day's agenda, the training diary, and an overview explaining how to rate their symptoms. To encourage compliance, preconfigured pop-up reminders were set, and site staff had access to the data in real time in order to identify if that patient was eligible to continue in the trial. This real-time monitoring was also available to the CRO and sponsor.

Results

Ninety percent of the 275 enrolled subjects utilized their own phones to submit their data at 16 timepoints per day for three days, two weeks apart. Ten percent of subjects used provisioned devices for various reasons (old phones, not smartphones, used work-provided phones and lacked permission to use, incompatible devices such as a Blackberry).

This study had an overall compliance rate of 98.3% with 86% of the subjects being 100% compliant. Another 9% of the patients missed one timepoint, demonstrating a 94% compliance rate. The remaining 5% missed two or more timepoints, making them 88% compliant or below. Most commonly, the last timepoint of the day was missed, which, depending on the patient's start time, may have coincided either with dinner time or bedtime.

Common Concerns Foreseen and Alleviated

In this trial, the common concerns with BYOD were easily alleviated, most often by ensuring that provisioned devices were available to the patients.

- Patient deleting app: The patient was on site for the first three hours, so the risk was small. Additionally, site staff who were monitoring the data in real time could notice if a patient wasn't complying and immediately follow up.
- Patient breaking or losing phone: The study lasted only six weeks, so this risk was small. Additionally, data collection always began on-site for the first three hours so a provisioned device could have been made available to the patient.
- Patient upgrading phone: The Lumenis app is upgrade compatible. No data would be lost if the patient upgraded, and the transition was seamless.
- Patient changing the time: Lumenis tracks the date and time stamp associated with each entry as well as the time zone, so if this occurred, site staff could follow up immediately.
- Patient forgetting password: Patients were screened one to three months before the study so they had time to reset passwords as needed. Additionally, provisioned devices were available.
- Patient unwilling to use own data plan: The data required for this study was minimal, making this less of a concern. Also, patients were allowed to use the site's Wi-Fi, and the app enabled patients to enter their data offline and then transmit later when Wi-Fi was available. Furthermore, provisioned devices were available to patients concerned about data usage.
- Bias possible: While there is a concern that BYOD could introduce bias by excluding that portion of the study population without smartphones, that wasn't the case in this study. This was a single study with a population compatible with smartphone users. Additionally, having provisioned devices available eliminated the risk for this study and can also alleviate that risk for other BYOD studies.
- Measurement equivalence concerns: The questions and all response options fit on the screen and did not require scrolling. The Lumenis technology maintains the format and adjusts it to fit on each device.
- Copyright holder unwilling to accept BYOD: In this case, Clinical Ink had made use of its partnership with Mapi and had successfully obtained permission from the copyright holder.

Conclusion

While BYOD is not appropriate for every trial, the advantages offered make it worth considering, despite the silence from the FDA. Sponsors or CROs considering a BYOD strategy would do well to consider using a qualified and BYOD-experienced vendor that can help evaluate the risks and opportunities — particularly one that can help them work through the regulatory concerns and with copyright holders, if needed.

In addition to helping determine the appropriateness of a BYOD approach, such a vendor should also be able to offer assistance and training to sites. Particularly when sites are unfamiliar with BYOD, a 24/7 helpdesk will ensure they have the support they need related to installing the app and training the patients. Upfront training is important, relating to handling smartphone upgrades, loss, or damage.

Your ePRO vendor should be able to proactively update its core software and also ensure that it aligns should patients upgrade their smartphones during the trial. The software should work on any Android or Apple iOS device and work seamlessly even if patients switch between provisioned devices and their own devices. Patients must be able to pick up where they last logged in, regardless of the device used.

Additionally, the software must enable consistency, which is key and especially important for equivalency. For example, Clinical Ink's Lumenis platform offers the interactive tools required to ensure patient education and engagement and it also provides configurable standard questionnaire controls: The date/time spinner, yes/no, vertical VAS, multiple choice, numeric rating scales, audio notifications, and more are all configurable. What this does is enable consistency regardless of whether a patient-provided device or a provisioned device is used.

To get some experience, researchers might consider working with their ePRO vendor to conduct a pilot and sensitivity analysis about BYOD within a study. Particularly for studies supporting primary end points and using homegrown questionnaires, researchers could gain valuable information by incorporating some questions asking patients about using their own devices. Performing exploratory, post-hoc statistical analysis could provide useful information on the classification of responders between the various modes used in the study while also comparing compliance rates.

While it is true that BYOD isn't right for all studies and that the FDA has yet to fully weigh in, researchers and CROs that fail to consider BYOD are losing an opportunity to save time, reduce costs, and provide more convenience to the patients in their trials. With guidance from an experienced ePRO vendor and deployed in the right situation, BYOD, or at least a hybrid BYOD model, offers advantages that should not be missed.

[1] Pew Research Center. Mobile Fact Sheet. https://www.pewinternet.org/fact-sheet/mobile/. Accessed April 29, 2019.

[2] Pugliese L, Woodriff M, Crowley O, Lam V, Sohn J, Bradley S. Feasibility of the Bring Your Own Device Model in Clinical Research: Results from a Randomized Controlled Pilot Study of a Mobile Patient Engagement Tool. Cureus. 2016 Mar; 8(3): e535. doi: 10.7759/cureus.535.

[3] Byrom B, Doll H, Muehlhausen W, et al. Measurement Equivalence of Patient-Reported Outcome Measure Response Scale Types Collected Using Bring Your Own Device Compared to Paper and a Provisioned Device: Results of a Randomized Equivalence Trial. Value in Health, 2018. https://www.valueinhealthjournal.com/article/S1098-3015(17)33615-X/pdf.

[4] Byrom B, Doll H, Muehlhausen W, et al. Measurement Equivalence of Patient-Reported Outcome Measure Response Scale Types Collected Using Bring Your Own Device Compared to Paper and a Provisioned Device: Results of a Randomized Equivalence Trial. Value in Health, 2018. https://www.valueinhealthjournal.com/article/S1098-3015(17)33615-X/pdf.

[5] Critical Path Institute. Electronic Patient-Reported Outcome Consortium. https://c-path.org/programs/eproc/epro-overview/best-practice-documents/. Accessed April 29, 2019.

Clinical Ink®

Confident Decisions, Faster

Direct Data Capture | eCOA | ePRO | eConsent

Clinical Ink, a global clinical technology company, offers data certainty from source to submission. Our eSource clinical technology and configurable ePRO and eCOA modules — a suite of solutions for capturing and integrating electronic data from sites, clinicians, and patients at its source — naturally enhance your clinical trial workflow by reducing manual labor, providing anytime, anywhere data access, and saving resources as your trials progress. Accelerate the completion of key clinical development milestones in your study and confidently manage your trial's critical decisions with our flexible menu of collaborative services, remote monitoring support, and a complete, real-time view of your trial.

Clinical Ink

Pennsylvania Office
110 Gibraltar Road, Suite 150
Horsham, PA 19044

North Carolina Office
525 Vine Street, Suite 130
Winston-Salem, NC 27101

Worldwide Inquiries

Phone +1.336.714.7402
Toll-Free +1.800.301.5033
Fax +1.336.464.2003
info@clinicalink.com

www.clinicalink.com