



CLINICAL
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Investigator Perspectives of Mobile Technology in Clinical Trials

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Agenda

Brief Background and Methods

Presentation of Interview Findings




- Perspectives on Advantages and Disadvantages of Mobile
-  in Clinical Trials
- Site Support Needs and Requirements
- Investigators' Lessons Learned and Suggestions

Open Discussion

The MCT Stakeholder Perceptions Project Team

- **Cindy Geoghegan, Patient and Partners**
- **Steve Morin, FDA**
- **Virginia Nido, Genentech**
- **William Wood, UNC-Chapel Hill**
- Maria Ali, The George Institute
- Annick Anderson, CISCRP*
- Ricky Bloomfield, Duke*
- David Borasky, WIRB-Copernicus Group IRB
- Angie Botto-van Bemden, Arthritis Foundation
- David Brennan, MedStar Health Research Institute*
- Kara Dennis, Medidata Solutions
- Sue Dubman, Individual Patient
- Guy Eakin, Arthritis Foundation*
- Terri Hinkley, ACRP*
- Les Jordan, Target Health
- Hassan Kadhim, Boehringer Ingelheim
- Kristine Nelson, EMMES*
- Amanda Niskar, Individual Patient
- Petros Okubagzi, MedStar Health Research Institute
- Ido Paz-Priel, Genentech
- Ken Skodacek, FDA
- Junyang Wang, FDA
- Immo Zadazensky, FDA*
- Amy Corneli, CTTI Social Science Lead
- Brian Perry, CTTI Associate Social Scientist
- Zachary Hallinan, CTTI Project Manager

Objectives

-  Describe site investigators' insights on the advantages and disadvantages of mobile clinical trials
-  Explain site-level budgetary, training, and other support needs necessary to adequately prepare for and implement mobile clinical trials
-  Describe site investigators' guidance for other site investigators who are interested in participating in mobile clinical trials

Methods

➤ **Dates:** June 8 to October 11, 2017

➤ **Participants:** Investigators (n=12)

- Had used mobile device to collect objective data in any kind of clinical

➤ research conducted in the U.S.

- Also had experience as investigator in traditional clinical research (i.e., not using mobile devices to collect data) with a clinical outcome

➤ **Method:**

- Qualitative, semi-structured interviews
- Conducted by telephone
- Digitally audio recorded with the participant's permission
- Transcribed verbatim following a transcription protocol
- Demographic information was collected

➤ **Analysis:** Qualitative applied thematic analysis

Study Population

Affiliation	<ul style="list-style-type: none">• Academic institutions (n=7)• Dedicated research sites (n=2);• Other (n=3) (clinical care and research organizations)
Years Research Experience	<ul style="list-style-type: none">• Traditional Clinical Research: 1-28 years• Mobile Clinical Research: 2-15 years
Specialties	Cardiology (n=2), Psychiatry (n=2), Hematology (n=2), Internal Medicine (n=2), Immunology (n=1), Neurology (n=1), Gastroenterology (n=1), Oncology (n=1), Endocrinology (n=1), Family Medicine (n=1), Other (n=1)

Types of Mobile Research

- Device Feasibility / Accessibility (n=9)
- Device Validation Studies (n=8)
- Observational studies (n=7)
- Phase III, registrational (n=6)
- Phase III, not registrational (n=6)
- Phase II a/b (n=2)
- Phase I (n=3)

Examples of Technology Used

- Continuous Glucose Monitor
- Activity and Sleep Monitor
- Electronic Pill Bottle
- Ingestible Sensor with Patch
- Mobile Spirometer
- Wireless Weight Scale
- Holter Monitor
- Implantable Cardioverter-Defibrillator

Experience with Real-Time Data

- **Most investigators had access to study data during the trial, but not all access was real-time**
 - Some access was periodic
 - Some access was dependent on when data were transferred from device to server
 - A few investigators had no access, per protocol
- **Participant access**
 - Half of investigators said participants did not have access to their data
 - Only two investigators said that they provided participants with real-time access to all of their data



Perspectives on Advantages and Disadvantages of Mobile in Clinical Trials

Advantages of Mobile Clinical Trials



Remote Data Capture

Investigators said that continuous and/or higher frequency data collection:

- Make it easier to understand participants' experiences
- Allow collection of data that studies typically are unable to collect
- Provide true compliance data (e.g., real world, metadata)



[Mobile devices] can serve as a really good, valid substitute of what could otherwise be very cumbersome process... there are times when you only valid option, the only rational option, is to use a mobile device.

Improving Study and/or Data Quality

Investigators said that mobile clinical trials:

- Are designed around study participants rather than researchers/research sites
- Provide better, more objective, higher frequency, and potentially more sensitive assessments
- Improve researchers' ability to deliver quality data
- Provide data that are easier to trust



[M]obile health trials allow us to recruit directly to the participant so it becomes more pragmatic, more real world, and hopefully with results that are more applicable

More Streamlined Study Operations

- Study participants can be recruited, enrolled, and managed remotely, which is easier for sites
- Data collection and management take less effort and costs less
- Monitoring and follow-up of participants can be done remotely (e.g., study procedures, compliance, adverse events)



...lessens the burden of having to bring patients back for every study visit... ensures, in many ways, a more continuous follow-up rather than this episodic follow-up... makes it easier to get key endpoints assessed within a follow-up window

Another Investigator Said:

The biggest benefit is just having access to it [real time data]. To have somebody who's being monitored at home, and being able to look at it when the participant has a problem. As opposed, the norm would be you get a phone call saying, "Hey I'm not feeling right," and saying, "Well come in tomorrow morning and see the research nurse, and we'll see what's going on." But instead I'm able to look and say, "Oh here's what's going on."



Other Advantages for Sites

- Having the ability to reach out to participants or conduct interventions as needed because of remote data capture and monitoring
- Can reach more participants
- Can intervene immediately
- Receiving automated notifications and reminders that help researchers stay in touch with participants and also help to improve participants' compliance

Advantages Specific to Participants

- **Real-time data:** Participants' access to real-time data can potentially drive engagement and satisfaction
- **Remove data collection and monitoring**
 - Automated notifications can help participants improve their compliance
 - Sites can reach and/or intervene with participants as needed based on real time data capture
- **Reduced participant burden and increased access to trials**
 - Participants do not have to be screened in person
 - They have fewer visits
 - The study is built around their convenience rather than the investigator's

“So to me the biggest thing is it opens up clinical trials to everybody, not just people who live close to an academic medical center, or a research center. It allows eligible patients that no matter where they live to often participate in a study.”

Disadvantages of Mobile Clinical Trials



Overall Disadvantages

- Increased time and labor spent managing and maintaining the devices, troubleshooting, and training
- Challenges with staff and participant acceptance
 - Learning curve
 - More technical training needed
 - May have reluctance from participants
- **Building rapport with trial participants is more difficult** because the direct interaction with participants is less
- **The burden of data collection has shifted to relying on participants** to use the device as instructed (potential to hinder recruitment and reduce data quality)



I think the technology is harder because you need to have staff that know how to deal with technologies like this. There's a learning curve for that.

An Investigator Said:

*Mobile data collection trials are many times more time consuming, and more complicated, and more burdensome, and so you're losing patients who might have said yes without that device or might have said yes with a simpler trial design. Those patients are saying no. **So there's a burden on the patients and there's a penalty to the industry** because we're losing some of those patients.*



Challenges Specific to Sites

Challenges from investigator **access to real-time data**:

- More time needed throughout day to review (often not reimbursed)
- System interfaces are not intuitive
- Connectivity problems

Study operations challenges:

- Following-up on missing data
- Burden from setting up devices and linking devices to specific users
- Having multiple consent procedures if use of the mobile technology was optional in the study
- Spending a large amount of staff time and resources maintaining devices—such as charging and storage, and diagnosing malfunctioning devices

An Investigator Said:

*Most of the portals are clunky. They're not intuitive. They're not mature pieces of software that now you sign in and, boom, you've got a dashboard, and the material that you needed is right at your fingertips, and your frequently clicked buttons over here in the lower left-hand corner. Instead, most of these pieces of software are data repositories and **they don't have a good user interface** and so it's difficult to find the data that you're looking for and to be able to look at the data that you're looking for.*



An Investigator Said:

In terms of the quantity of patients in research trials, what percent of the patients have tech support problems? Less than ten percent.

*How much time does it take of clinic staff when patients have tech support problems? That's where it might actually be a burden that's more than ten percent **because it's incredibly time consuming to fix that one problem.***



Investigators Said:

So they shift that burden to sites. So we then have to learn that system, to train on it, to train our patients on it, to keep up to date, to keep those units charged, to keep them properly stored, properly inventoried, and then troubleshoot, should they go bad, which they do.



We have so many devices. They're everywhere. Each device has its own power cord and its own way of uplink. There's a tremendous burden on the site in terms of training on all of these individual devices, and upkeep of the devices, and storage for all the devices. There's a huge burden that right now the sites aren't being compensated for...



Challenges Specific to Sites (cont'd)

➤ Challenges with **adoption barriers and lack of familiarity with mobile technologies**

- Difficult for participants to use some technologies as intended for trial
- Dislike of technology used can lead participant to view trial poorly
- More time needed to train staff and participants

➤ **Data quality challenges**

- New data biases
- Data quality can be hampered by continual technical challenges
- Need to ensure proper data attribution

➤ **Industry hasn't "matured"** to a point to provide adequate rules or guidance on how to deal with challenges (e.g., missing data) or best practices in incorporating mobile technologies

Challenges Specific to Participants

- Participants are asked to bear more of the study-related burden (data capture, device/technology management and upkeep)
- Real-time access to data could impact participant behaviors, especially if device reports inaccurate data, participants cannot interpret data, and/or participants don't see improvement over time
- **Using and interacting with the technology**
 - Unfamiliarity with or concern about using certain mobile technologies may inhibit participants from joining the study or misusing the technology
 - Certain technology may be viewed as more invasive
 - Device malfunctions throughout the trial may frustrate participants
- Inadequate IT support, not trained to communicate with the patient-participant population

Investigators Said:

*I think the biggest problem was that you're returning data that is very complicated, that was in a report form that is designed for physicians to read... **And so I think the biggest challenge was to be able to explain each individual's results in a scalable way.***



*I think that **if you have a participant who is, for whatever reason, frustrated with the device or having technical problems with the device, that person may actually become less engaged** with the study or may even drop out of the study would be a potential concern.*



Summary Perspectives on Mobile Trials

Advantages

- Potential to reach more participants and conduct desired research because the study can collect data remotely
- Potential to increase adherence (e.g., objective monitoring of compliance, automated notifications and reminders)
- Can decrease participant burden (e.g., fewer visits, remote screening) and drive engagement
- Can improve quality of study and data collected

Disadvantages

- Usability issues and added requirements for patients can hamper recruitment, adherence, and retention
- New operational challenges for site staff, such as training, troubleshooting, and maintenance needs (e.g., space to charge devices)
- Real-time data creates new expectations on site staff (e.g., review throughout the day, investigating causes of missing data)
- Potential data quality issues, including both technical issues and the potential for new biases (e.g., patient behavior change due to device use)

Questions / Comments?



Site Support Needs and Requirements

Investigator/Staff Time Requirements

- Numerous investigators (but not all) stated that mobile clinical trials required more of their time in comparison to traditional clinical trials
- Additional time needed for:
 - Having more data to monitor and review
 - More training to attend
 - More time interfacing with software
 - Longer visits (participant education / re-education, troubleshooting devices)
 - Having fewer staff requires more of the investigator's time
- Novelty of such research requires a learning curve

An Investigator Said:

If you're on one clinical research trial and you're just trying to dabble in research, maybe it's not that big of a deal. If you're on 55 concurrent trials, it's a huge deal.

You're spending so much time in trainings, and re-trainings, and re-trainings, on all of these various pieces of software, and they're competing with each other...We've got multiple trials with multiple different sponsors all with their own devices, and so we're doing individual trainings on individual devices that are all doing exactly the same thing.

*They all have their own cloud-based portal that we have to use, just **a tremendous burden, and things like that suck the fun out of research.***



Troubleshooting

- Numerous investigators described that troubleshooting occurred frequently in their research
- Typical problems included:
 - Device failures
 - Device loss
 - Poor penetration or connectivity
 - Newness of the particular technology
 - Having to troubleshoot independently in the absence of an accommodating or qualified call center

An Investigator Said:


It depends on the device, honestly.

*We usually learn that pretty quickly early in the conduct of the study. **So for example, if we're having problems with a charging situation on a device; or we're having problems with getting these devices initially synced, and getting the data calibrated enough, and getting it uploaded, I think we learn that pretty early on.** And then I think if it's—tips that we find—solutions that we find allow us to address it more efficiently as the study goes.*



Budget: Being Prepared


- ▶ Numerous investigators said they were inadequately prepared to plan a site budget for a mobile clinical trial when they were first approached by a sponsor
 - Underestimated staff time for troubleshooting and participant support
 - Device-related costs were an afterthought



In terms of budget, we had no clue how much time [would be] consumed by the staff coordinators and other staff members and total learning experience for us.

Budget: Biggest Expenses

- ▶ Additional staff time required for mobile clinical trials was the biggest additional expense
 - Managing the devices: troubleshooting device issues, dealing with device failures, or interacting with tech support
 - Training participants



[I]n a year study, you might end up spending 2 hours per patient of coordinator time to train for a particular study for a device. And if you have 10 patients in that study, that's 20 hours. Well, that's half a week with that.

Budget: Other Costs

- The direct cost of purchasing their own devices and the software needed to connect to the devices (for investigator-initiated research)
- Costs for managing device loss, or malfunctioning or broken devices
- Storage of both pre-use and used devices Device rental when devices were not available
- Set-up fees associated with the use of some devices
- Paying an outside vendor for tech support and data management
- Having study staff conduct participant data monitoring

Important Planning Considerations

Budget

- Most additional costs are device related:
 - Increased training costs (e.g., use of devices, portals)
 - Time training patients on device and troubleshooting
 - Device set up, storage, and repair

Time

- More time needed to interact with patients
- Less time needed for study visits, data entry, and scheduling
- Staff spend LOTS of time solving device problems

Training

- Helpful for site staff to have:
 - Hands-on training with device
 - Refresher trainings
 - Training conducted immediately prior to trial initiation

Support

- Need support from device manufacturers, vendors, and internal IT department
- Tech support should be device savvy and timely, but also knowledgeable about the study population

Questions / Comments?



Investigators' Lessons Learned and Suggestions

Device Selection and Study Operations

- **The clinical trial should not be designed around a device:** all technology use should be appropriate and justified
- **When selecting a mobile device:**
 - Select a device that is most appropriate for the user population
 - Sponsors should seek investigator input
 - Conduct a technology assessment on all options
 - Devices should be thoroughly tested under realistic conditions
- **Study planning and execution:**
 - Ensure sites have appropriate infrastructure and provide support
 - Have policies to handle device loss / malfunction and data loss
 - Provide more devices to sites that are historically adept at enrolling
 - Ensure tech support is easily accessible throughout the life a trial, staffed by actual people, and centralized
 - Make devices easy to return at study completion

An Investigator Said:

*Reducing the complexity would absolutely help. We're making trials more complicated. **We're making more procedures per patient per trial and then you're adding devices and technology on top of this.***

*It's all fun and games when you're designing the protocol, and everything seems cool, and you can geek out over how great this is going to be, but **we as an industry need to take a step back and say let's simplify this because patients need to do this, and investigative sites need to be able to conduct this, and we're trying to squeeze too much into one protocol.***



Addressing Participant Burden

Mobile clinical trials should be participant-centered

- Include patient input from the outset, including in trial design and value of research
- Ensure that any additional burden from technology use is truly necessary for the research
- Consider varying support needs of different patient populations
- Investigators should ensure that they fully understand what is required of participants to take part in the study

Technology/devices should be:

- Appropriate for the patient population
- Engaging, user-friendly, simple, and streamlined to reduce patient burden

During the trial:

- Ensure periodic check-ins to address any developing questions
- Involving a participant's family or friends can aid in technology use

Training for Site Staff and Study Participants

- **Similar considerations for both site staff and study participants:**
 - In-person, hands-on training is important
 - Trainings should be available in several formats to suit varied learning styles
 - Ensure resources are available to answer questions or provide refreshers after the initial training
- **Additional considerations for training site staff:**
 - Explain how best to handle device malfunctions
 - Help staff have more empathy for participants
 - Additional training may be needed if real-time data is being provided
 - Do not require re-trainings for devices that sites have already used
- **Make devices simpler**

An Investigator Said:

Ideally, you make the device and the trial as simple as possible** so as little as possible of the burden of understanding the device and how to make it work is on the patient, so for the patient, it's as simple as possible. **They put it on, and they wear it, and that's their role.** But I would definitely focus more on making it as simple as possible for the patient **and cut down training with patients.



Tech Support for Investigators and Staff

- Numerous investigators described **support needed from sponsors**
 - Assistance with device-related issues, such as a call center
 - Provide a third-party vendor hired to troubleshoot device-related issues
 - Device training
- A few investigators described **support needed from device manufacturers**
 - Technical support for initial set-up, participant monitoring, data management, and troubleshooting purposes
 - Support in procuring the devices needed for the study
 - Internal IT support (e.g., helping staff to interface with the data collected from the devices; linking the device to a software platform, or to have various types of software interface with one another)
 - A call center

Addressing Budgetary Challenges

- Sites need to be fully compensated by sponsors for the increased time, staffing, troubleshooting, and financial demands of mobile trials
- Investigators should be aware of increased costs: Sites should create their own budgets and then compare to budgets offered by the sponsors
- Budgets should be clear and fair, and ensure provisions for:
 - Device storage
 - Staff time for training (for site staff and patients) and troubleshooting
 - Increased time to contact and monitor participants outside of office visits
 - Sponsors should allow some flexibility in budgeting, as many costs are unknown at the time the budget is created

Addressing Contract Challenges

- **Ensure clear delineation of responsibilities** of all parties involved in the contract (including responsibility related to device/technology problems)
- **Investigators should know that the contracting process is more complex and takes more time** due to unknowns inherent in the use of new technology
- **Contracts should include a line item for technology-related costs**

Summary of Investigators' Top Lessons Learned

➤ **First and foremost: Ensure device use is appropriate**

- If it is, sponsors should obtain sites' feedback on device *selection*, and patient feedback on device *use*

➤ **Be prepared!** Mobile clinical trials may initially require extra staff time and funding, and a plan is needed for technology malfunction

➤ **Streamline and centralize processes:** training, data collection

➤ processes, and results (e.g., seamless integration with EHR, software)

➤ **Consider implications for study data**

- Concern with potential study population selection bias due to wireless access and technology literacy
- Be conscious of participant behavior change due to device use, including changes in the real-world use of the device because of additional interaction with staff to troubleshoot tech issues

Discussion

1. Do the findings from the investigator survey align with your experiences? (Why or why not?)
2. In thinking about optimizing mobile trials of the future, should we be thinking about different categories/types of mobile trials, or mobile trials as a whole?
3. What are the most important takeaways that could form the basis of recommendations for the research enterprise?

THANK YOU.



Bill Wood, University of North Carolina



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