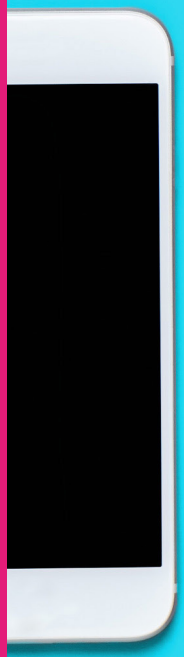
PRA Health Sciences

WHITE PAPER

Decentralized Clinical Trials: The Call for a New Paradigm



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Introduction

The existing framework around modern clinical trials is antiquated and inefficient. The foundations for clinical development date back to the 1938 US Food, Drug, and Cosmetic Act which gave the FDA authority to ensure drug safety. It was later amended by congress—The Kefauver-Harris "Drug Efficacy" Amendment of 1962—which required that drugs be proven efficacious and safe before being sold, and that it was the FDA's authority to oversee safety and effectiveness was that of the FDA. Now, 40 years later, we're running clinical trials almost the same way we did when we started.

The world and technology, on the other hand, are passing our industry by. Digital tools continue to advance while clinical research remains slow to embrace efficient platforms and offerings. The result is a market where a new drug costs in excess of $2 billion and takes over 10 years to get to market – if it even makes it to market.

Fixing the current paradigm and ensuring that every patient gets access to the best possible care is a moral imperative. This white paper considers how incorporating more virtual/hybrid trials and decentralized research into clinical development can better integrate healthcare into patients' real lives and accelerate approval of new medications.

Terminology

Traditional Trials are trials that are 100% site-dependent. Activities conducted onsite include:

- Periodic patient visits
- Laboratory tests
- Drug distribution
- Device allocation
- Physician consultation
- Nurse and site staff assistance
- Patient-related data collection
- In-person informed consent

Hybrid Trials are trials where the site dependence varies. Activities conducted onsite or offsite include:

- Patient check-ins
- Routine tests conducted
- Drug distribution
- Device allocation or shipment
- Physician consultation
- Combination of virtual and onsite consulting
- Nurse and site staff assistance
- Combination of mobile nursing, telemedicine, and onsite nursing
- Patient-related data collection
- In-person or using eSource

Fully Virtual, Mobile or Decentralized Trials are trials where there is no site dependence, but meta-sites exist:

- Utilize telehealth and telemedicine
- Patients do not visit sites
- Mobile healthcare providers are allies
- Tests conducted virtually, at community laboratories or mobile nurse-aided facilities
- Drugs and devices are shipped to patients' houses
- Virtual physician consultation—text, audio, video
- Virtual/in-home nurse assistance
- 24/7 patient support
- Patient-related data is collected virtually or mobile healthcare providers-aided
- Telehealth or mobile informed consent

Current Clinical Research Paradigm

The industry unwillingness to adopt innovative changes is partly because the current model took a long time to build. Thousands of working processes depend on this paradigm. The technology we have today didn't exist when we built the current model. Despite many technological and telecommunications advancements, the healthcare industry is slow to adopt change. For example, it took 25 years for the industry to move from using paper to electronic medical records. The push for a new model is crucial to executing successful and efficient trials.

There are disruptive innovations that could make the process quicker. However, continued reluctance to adopt innovative approaches among some sponsors and clinical research organizations exists because we work in a regulated industry, and many approach change with caution. The current business model is not sustainable; it's incompatible with the positive, disruptive changes that everyday technology enables. The more time and money spent in clinical development, the more patient lives are at risk.

Drawbacks of the Current Model

Since the 1980s, there have been limited changes to how we develop drugs in their clinical development. The FDA is in the process of modernizing, but legacy frameworks are slow, costly, and burdensome, and continue to be constrictive. The current system and clinical research protocols require many on-site procedures that take up patients' time. The average patient cannot take one day off each week to participate in a trial—as a result, today's trials are not in line with the standard of care. The majority of protocols today have two to five times the number of procedures or visits a patient would receive for their disease management in the normal course of care. As a consequence, this makes the patient burden too high, making it difficult to recruit and retain clinical trial participants. Patients must journey to sites that may be far from their homes—an average travel of two to three hours—when they could instead pick up a prescription at a nearby pharmacy. As a result, only about three to five percent of eligible patients get to enroll in clinical research and there is a 30% dropout rate for those who do enroll across all clinical trials.

With the existing model, it is difficult to recruit and keep patients in clinical trials. The vast majority of today's population are millennials who use digital technology daily for nearly all forms of activity—entertainment, shopping, hailing a cab, etc. As a result, they expect healthcare to maneuver the same way. While the healthcare system is taking steps towards integrating technology—for example, telehealth—there has been little movement in the clinical trials space. As a result, patients are less willing to partake in clinical trials that do not utilize some mobile form of technology. Studies show that about 75% of people preferred a mobile trial over a traditional trial, and 80% of patients are more likely to take part in a trial that uses mobile technology[1].

The Status Quo is Costing Patient Lives

Study Details

80 adults with chronic pain
(pain for ≥3 hours a day and rated ≥4 on a 10-point scale)

40 to a paper diary

40 to an electronic diary

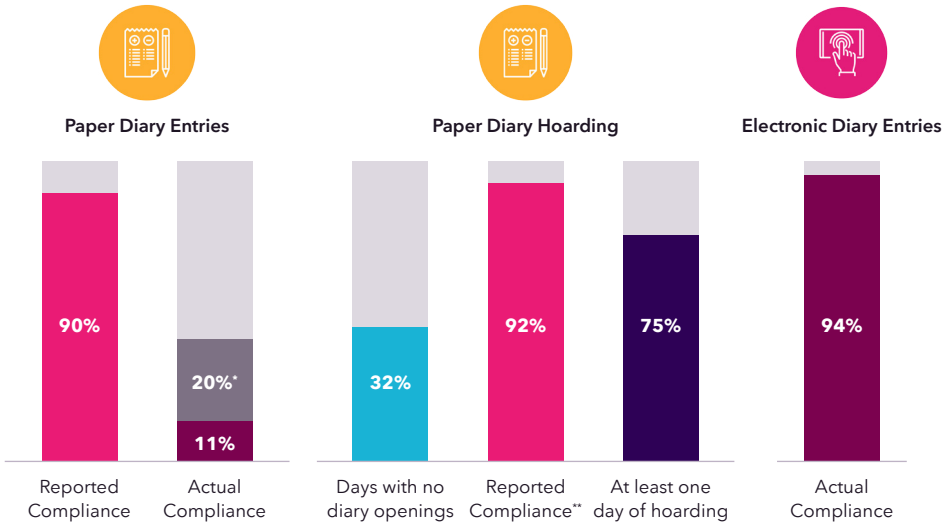
Daily entries at 10AM, 4PM, and 8PM within 15 minutes of the target time
(electronic entries could not be initiated outside 30-minute windows)

*Actual compliance with 90 min window
**For days with no diary openings

Observations

Paper diary entries were deemed compliant if the binder was opened or closed at any point during the target time window. We also assessed "hoarding" with the paper diary, defined as days when the diary binder was not opened but for which diary cards were completed.

Results



It's not just recruiting and retaining patients that is difficult using the current model. Studies show that, without technological tools, data is often noncompliant. For example, 20-30% of patients do not adhere to their medication regimens that are curative or relieve symptoms. Between 30-40% of patients fail to follow regimens designed to prevent health problems, and 50% of patients fail to adhere to their long-term prescribed medication. The result of these failed drug adherences is billions of dollars in failure cost to pharmaceutical companies. On the other hand, patients were 94% compliant when their diary entries were electronic vs. paper diary entries at 20%[2-3,7]. Virtual engagement can significantly impact drug adherence and patient behavior, saving time and money that could be better spent on developing treatments that improve patient lives[4].

The Need for a New Model

Given the challenges of our current model, the industry must be proactive in adapting today's technology and digital health platforms to incorporate into clinical trials, making them more efficient, safe, convenient, and cost-effective.

What do we need?

- There's a push by patients to use telemedicine and digital engagement for their healthcare interaction. The healthcare industry needs to incorporate today's technologies into how we run clinical trials.

How do we do this?

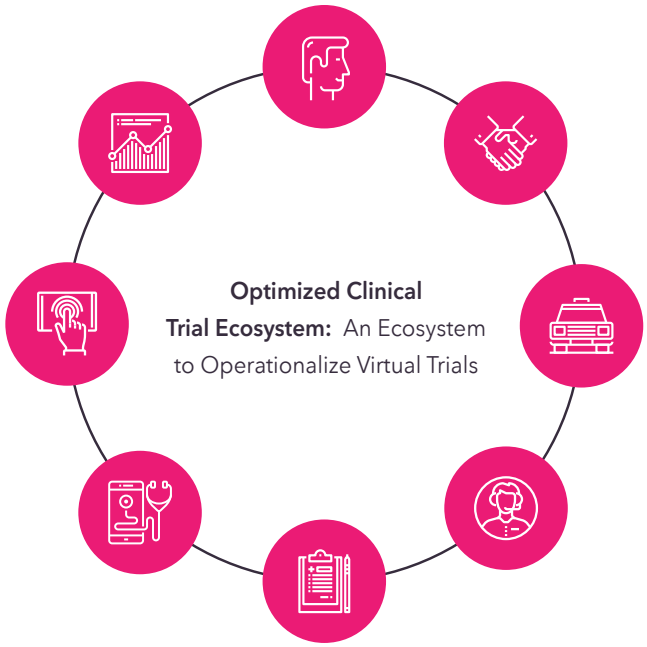
- Create a mobile platform that is regulated and allows patients to participate in clinical trials, and collects data for a trial in a digital environment to make it more congruent with how their healthcare is delivered.

Data
- Patient data
- Insights
- Real World Evidence

Technology Platform
- Patient facing
- Mobile Healthcare Provider facing
- CRO-Sponsor friendly

Mobile Healthcare Providers
- Mobile Nurses
- Telemedicine capabilities
- Online physician consultation
- Causality crew

Regulatory Bodies
- Right IRB
- On-board early



Patients
- Patient engagement
- Enhanced patient experience
- Patient adherence

Vendor Partnerships
- Wearables
- Devices

Supply Chain
- Device provisioning
- Drug distribution
- IP storage
- Drug/Device kitting

Patient Support Call Center
- 24/7 IT support
- Troubleshoot
- Multi-language assistance

What would it look like?

- Maximizing patient recruitment with regional, state, or country virtual models.
- Using virtual and hybrid trials to reduce cost and resources with siteless, distributed, and hybrid clinical site models.
- A new circle of care: Through their device, the patient would have access to caregivers (who manage care, develop relationships), friends and family (to provide emotional support and motivation), CRC/Site (for day-to-day patient management, oversight, and engagement), sponsor and CRO (oversight of study management, concierge services, and study analytics), mobile HCPs (home or work visits for participants screening and follow up visits), and PI/HCPs (telemedicine visits, AE management and assessment, clinical oversight).
- Mobile Patient Engagement: Anywhere, BYOD, personal mobile devices are preferred form of connectivity.
- Using technology to partner with the FDA to create new validated endpoints.

What would a new model offer?

- Real-time patient data insights.
- Enrollment insights–dashboards show what is/not working and when to stop recruitment.
- De-risk trials in real-time–compliant patients, fewer patients needed, faster database lock.
- Enhanced patient safety–clinical team alerted to adverse events as soon as they occur, direct to patient notification.
- Patient-centricity and empowerment–informed and educated patients know what to expect and are more compliant.
- On-demand support–click-2-call, live chat, telemedicine, home healthcare, travel (Uber, Lyft, etc.).

FDA Commitment to Innovation

In recent years the FDA has demonstrated an open stance towards new ideas and technology innovations. With the issuance of new guidance such as the Digital Health Innovation Action Plan of 2019, the agency acknowledged that "digital technology has been driving a revolution in healthcare" and indicated that use of smart phones, social networks, and internet applications providing innovative ways for us to monitor health and well-being should be used more broadly[5]. The FDA-sponsored Clinical Trial Transformation Initiative has published recommendations for conducting decentralized clinical trials through telemedicine and mobile healthcare providers[6]. By understanding the convergence of people, information, technology and connectivity to improve health care and health outcomes, the FDA is perhaps more progressive then conservatively-minded sponsors and drug development organizations.

We should take advantage of the FDA's positioning around mobile health, health information technology, wearable devices, telehealth, and telemedicine to re-write how clinical development can be done. Our industry should examine each new protocol in order to make them more patient-centric by incorporating mobile technology and employing the virtual, hybrid or decentralized models.

Conclusion

With technology being used daily by most of the population, clinical research needs to take the initiative to incorporate mobile platforms in their studies, and to execute more virtual and hybrid trials. Doing so will reduce billions of dollars in excess costs, reduce the burden on patients who otherwise would be traveling to sites, increase recruitment rates, allow for cleaner, more robust data, get drugs approved faster, and, most importantly, save patient lives.

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Contact Information

For further information, or to discuss any aspect of PRA's services offered in the field of decentralized clinical trials, please contact your Business Development Manager or the corporate office below:

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