ELLIGO HEALTH RESEARCH® | Goes Direct®

The Power of Technology-Enabled Services

Shifting the Research Paradigm in Response to a Changing World

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Introduction

The disconnect between clinical research and medical care has become increasingly burdensome, especially in the wake of the COVID-19 pandemic. As clinical research sponsors continually seek ways to accelerate their trials while maintaining safety and quality, technology remains underutilized in research, despite remarkable technological advances in the past 20 years. Achieving the desired benefits could be a matter of leveraging technology-enabled solutions and services that place more control closer to the source.

For years, paper-based processes have provided a path of least resistance with electronic data capture automating, but essentially mimicking, the paper processes. This resulted in more rapid database locks but study coordinators and patients have not reaped significant benefits. Physicians have hesitated to offer clinical research to their patients due to these time-consuming processes and the initial requisite investments in infrastructure, resources, and training.

For clinicians who do invest in research, The Coalition for Clinical Trials Awareness reports that 11% of sites fail to enroll a single participant in trials they agreed to conduct.

This is not a new phenomenon. For patients, access to research as care option may not be feasible because of logistical concerns such as time spent traveling to a research site, the associated costs, and missed work hours. Data from Citeline and Clinicaltrials.gov indicate that a mere 1.5%–3.0% of the eligible population — including both potential patients and administering physicians — will participate in a clinical trial. This perpetuates the challenges researchers face in enrolling participants in protocols and reaching diverse populations.

For these reasons and more, the U.S. Food and Drug Administration (FDA) has been encouraging “modernization of clinical trials” in response to the 21st Century Cures Act and statements made by former FDA Commissioner, Dr. Scott Gottlieb, accusing the clinical trial establishment of adopting a model that is not “compatible with

the kind of positive, but disruptive, changes that certain innovations can enable." The Cures Act also encourages the use of real-world data (in addition to that from clinical trials) for FDA decision-making, halting information-blocking, and placing patients in control of their health information. The U.S. Department of Health and Human Services' (HHS) Office of the National Coordinator (ONC) is leading the effort on the latter two objectives. Regulatory and policy changes such as these, combined with the recent global COVID-19 pandemic, have spurred research sponsors to consider new ways to conduct clinical research in this changing environment.

Shifting the Clinical Research Paradigm

Decentralized clinical trials (DCTs), virtual trials, "siteless" trials, and hybrid trials have been discussed, piloted, and conducted by some companies over the past decade. Unfortunately, there have been varied definitions used when describing these trial types or applying these terms. At this point in time, Elligo is choosing to use the terms as introduced by the FDA (Dr. Isaac R. Rodriguez-Chavez, 2019) where:

- **Complete DCTs** are understood to have all trial activities decentralized
- **Hybrid DCTs** have a decentralized component
- **Virtual trials** are understood to be those that are conducted without patients (e.g., computer simulations or computer modeling)

The terms "site" and "siteless" are intentionally avoided here; rather, the importance is placed on the investigator and his/her relationship with the patient instead of a physical location.

In the wake of COVID-19, many sponsors were forced to plan for business and research continuity scenarios if in-person visits were not an option. Contingency plans and additional capabilities were required to ensure research resilience, often relying on telemedicine and other tools that reduce the dependency on physical sites and in-person patient visits. Beyond connectivity to technology and the patient's level of technological sophistication, the ability of a patient to physically leave their home also presented unique issues as shelter-in-place orders were implemented during the pandemic.

However, these physical restrictions did not mean the complete shutdown of clinical research for prepared sites as over-the-phone or virtual telehealth visits could be carried out to ensure the safety of all parties and continuation of research studies. Additionally, since physical site access was restricted, many CRAs could not monitor on-site. Paperless research sites with cloud-based electronic regulatory documents and electronic source (eSource) documentation systems enabled a transition to remote monitoring. To facilitate more collaboration between coordinators and CRAs, electronic collaboration capabilities and videoconferencing have been used. Protocols were also modified to accommodate changes in visit frequency and types of visits required. The FDA has provided and regularly updated new guidance during the pandemic on how to continue clinical trial conduct.

Moving into the future, sponsors must be prepared to grow and adapt to the coming changes while also preparing to train personnel and provide appropriate equipment to meet changing requirements. The changing environment has necessitated rapid adoption of some new technologies which have ultimately proven to be efficient and effective in facilitating a new paradigm for clinical research. While there are still challenges to conducting complete DCTs, especially for certain protocols, the pandemic seems to have stimulated adoption of technologies and processes that can help modernize the clinical research enterprise.

The paradigm shift is, therefore, to integrate more control into the front end of the trial — into the hands of the patients and investigators. With this in mind, Elligo has developed a system to fit research into the existing workflows of healthcare, rather than trying to force healthcare processes to conform to research protocols. This is a patient-centric approach that maintains and places value on the physician-patient relationship; it not only focuses on people and

processes, but also leverages technology to bring research where it needs to be, whether that is in the patient's home or in the healthcare clinic. Elligo is a healthcare-enabling research organization that enables community practices and clinicians in various patient care settings to conduct high quality clinical research. Clinical research should provide a mutually beneficial opportunity: When patients gain access to the latest research and treatment opportunities, clinical research serves to decrease the overall cost of care for the patient and infrastructure costs for the investigators. Ideally, this opportunity bridges research and healthcare in a seamless manner.

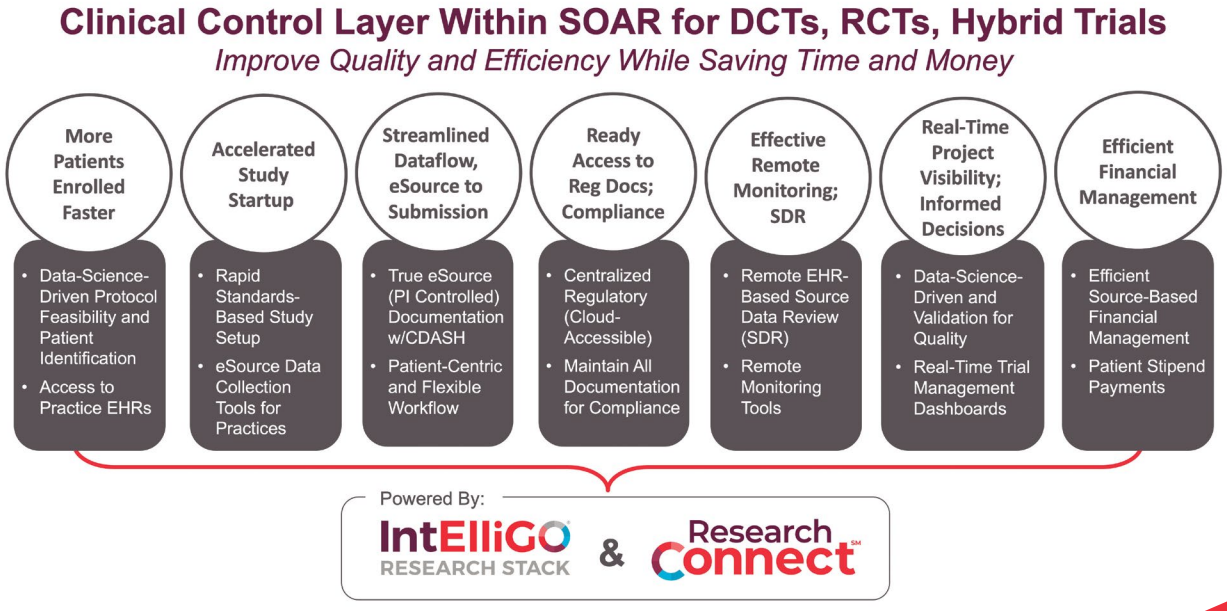
The Role of Technology in Realizing a New Clinical Research Paradigm

In the age of technological adoption across many industries, it is easy to assume that physicians and patients have access to computers and internet connectivity. When this is not the case, it can create major barriers to study workflows, patient participation, and participant diversity. As we develop processes to solve challenges patients face when accessing technology, it is important to consider that, just as there is no one-size-fits-all approach to patient treatments, there is no single approach to technological adoption. During the pandemic, physicians and patients became more familiar with technology while working remotely; many may choose to continue to use telehealth visits with physicians going forward. Researchers must develop innovative solutions and a system that works across patient populations to bring research as a care option to all patients, not just a select few.

Technology is never a solution in and of itself. It is important to ensure that, when technology is applied, it must be accepted by users and the processes it automates must be streamlined or redesigned, versus automating old paper-based processes; this cannot be overemphasized. Also critical is where the "control" is placed when technology is applied. This particular concept was discussed at length when 21CFR11 became a regulation. One of the regulatory requirements for electronic source data/eSource documentation is, "The sponsor shall not have exclusive control of a source document," where control is defined as, "The ability to decide when source data are created, amended, viewed, or copied." This one requirement generated more discussion than the remaining eleven. Control is a very important concept in clinical research, especially as it relates to patient data. While sponsors must be in control of their research programs, they must ensure that there is a clearly traceable path between the patient data collected in support of new product approval and the data the regulators (medical and statistical reviewers) see in the submission, including a record of any changes made during that route (i.e., the audit trail). The investigator must be responsible for (in control of) the research data.

As a healthcare-enabled research organization that provides technology-enabled services, Elligo ensures that there is a trustworthy control layer where it matters — with the patient and his/her physician. Yet information about the research study is continuously and immediately available for research sponsors to access and follow at any time. This customized control removes many undue burdens from the sponsor.

The figure below depicts the key features (in rectangles) of the clinical control layer (CCL) that Elligo enables, along with the value (in circles) that each of these features brings.



Investing in a System of Accelerated Research for the Future

Elligo has developed a continuum of technologies and data science capabilities to enable patients, clinicians, and sponsors to conduct more efficient research. These are paired with streamlined processes and experienced personnel. This system of technology-enabled services can support complete DCTs, hybrid DCTs, and traditional randomized clinical trials. It relies on access to and use of real-world data from EHRs and can incorporate patient-reported outcomes and other patient-entered or third-party data, if appropriate.

Taking advantage of industry standards from the start has been reported to decrease study startup time by 70%–90%.

Elligo's technology-enabled services system was developed to be flexible and adaptable, with the patient and the investigator at the heart of the design. It was also developed to redesign the research process, focusing on key concepts, which were presented by Dr. Janet Woodcock at the 2018 Bridging Collaborative and are necessary to better bridge clinical research and healthcare:

a) The patient and the physician are at the center

b) Quality and standards-based data are integrated from the start

c) Workflow is centered on the patient and healthcare provider

d) Informed consent is integrated and the process simplified

e) Learning health cycles are more rapid

These concepts are the basis for Elligo's System of Accelerated Research (SOAR™), which not only mitigates risk, but adheres to regulations and improves data quality while decreasing resource requirements and costs associated with clinical research.

SOAR components that provide Elligo's clinical control layer include:

- Engaged physicians/investigators, with 88% of physicians polled expressing interest in conducting a SOAR trial
- Patient recruitment driven by Elligo's ResearchConnect EHR data
- Rapid study setup in days with IntElligo® Research Stack, leveraging the CDISC protocol-representation model (PRM)
- Staff with training in regulatory requirements who maintain the necessary regulatory documents electronically using Florence Investigator Site File technology
- eSource documentation with CDISC/CDASH, eliminating error-prone transcription
- Study management dashboards, tools, and experienced personnel to oversee medical monitoring and patient safety
- Technology to support remote monitoring and source document verification
- Tools and methods for facilitating financials and communications
- The ability to provide data in submission-ready formats

Elligo leaders are experienced in applying the governing regulations and able to customize Elligo's SOAR model and technology-enabled services to accelerate research without compromising quality and integrity. The integration of Elligo's technology components with the SOAR processes and trained staff provides a pathway to conducting DCTs or hybrid DCTs and modernizing clinical research for a new paradigm in a new age of clinical research.

Conclusion

A changing environment with heightened concern for the safety of patients, healthcare providers, and clinical research staff has stimulated a more rapid acceptance of certain technologies that facilitate the modernization of clinical trials and a new paradigm for clinical research. This is a perfect time to step back and review the current clinical research process so that we can redesign it to not only meet new requirements, but to leverage technology. A System of Accelerated Research with technology-enabled services can be customized to optimize the implementation of any given research protocol, and especially when underpinned with Elligo's clinical control layer, can be mutually beneficial for sponsors, physicians, and their patients.

About Elligo Health Research®

Elligo Health Research, a healthcare-enabling research organization, uses electronic health records and the trusted patient and physician relationship to ensure all patients have access to clinical research as a care option. Powered by our *Goes Direct*® approach and novel IntElligo® Research Stack clinical technology, our team provides access to the best healthcare experts, patients, and research technologies. We engage physicians and patients who otherwise would not participate in clinical research and accelerate the development of new pharmaceutical, biotechnology, and medical device and diagnostic products. Learn more at elligodirect.com.