

# Integrated clinical research—A new operating model to enable research as a natural output of clinical practice

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## Introduction

Medical science has undergone a dramatic shift in the last 30 years.

Our understanding of human health has been transformed through major advances in disease diagnosis, as well as new treatment paradigms such as live transplantation, immunotherapy, and gene splicing. Alongside these changes, many health services are being digitized. Technologies such as robotic surgery, three-dimensional bioprinting of bones, organs, and teeth, and cutting-edge new appliances are changing how medical professionals deliver care.

In addition, in 2009 the American Recovery and Reinvestment Act (ARRA) and HITECH included \$19.2 billion to fund Electronic Medical Record (EMR) implementation for physicians and hospitals.<sup>1</sup> Over the past 10 years ARRA has catalyzed the widespread adoption and use of EMR systems, electronically documenting physician-patient interactions at the point of care. As healthcare digitization expands, availability of valuable medical data has increased exponentially, enabling medical professionals to view the human body as a “big data” platform, full of measurable patterns and life-saving insights.

Despite these compelling advances, time-to-market for new therapies and the cost for medical research and development are continuing to increase.<sup>2</sup> The last 20 years have seen a significant increase in the amount of data collected for each trial participant, often without any proven additional benefit. Inefficiencies within the current research operating model are well documented.<sup>3</sup> In a November 2018 industry panel, Janet Woodcock, Director of the FDA’s Center for Drug Evaluation and Research (CDER) is reported as declaring “I believe the clinical trial system is broken...I do not believe it serves the interests of patients.”<sup>4</sup>

Figuring out how to more effectively reduce unnecessary time and resource spending without sacrificing the integrity of groundbreaking studies is critical to the future of medicine. Many of the inefficiencies in clinical research are the result of an outdated operating model, developed in an era where external sources of digital healthcare data were not available. The current model is study-centric, where each study produces the data it needs to answer a specific research question.

This paper proposes a new operating model for clinical research, primarily by taking advantage of healthcare digitization and integrating research fully at the point of care.

With the right technologies and compliance framework to support this new model, there is a compelling opportunity to dramatically improve the efficiency of clinical research. In turn, this new model will ensure that the next generation of life-saving therapies can be developed faster and cheaper while retaining or enhancing current standards of scientific rigor.

## Clinical research—an operating model under stress

The fundamental models used to conduct clinical research have changed very little in the last half century, despite shifts in our understanding of medicine and sweeping changes in how it’s being practiced.

The current research operating model grew out of individual study workflows, making it largely disconnected from routine clinical practice and modern, real-world care delivery systems. It was originally designed to support interventional randomized clinical trials, which involve carefully selected cohorts of patients and are designed to test the efficacy or safety of a treatment.

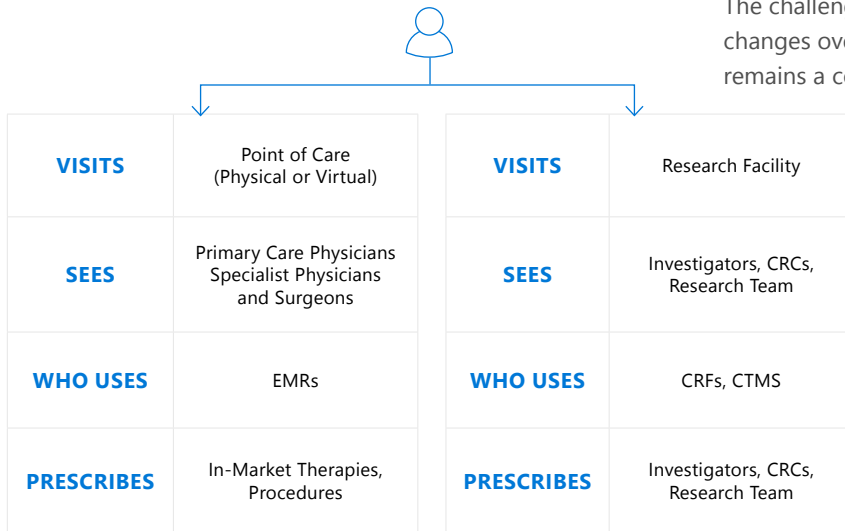
In an interventional clinical trial, a study protocol drives the de novo capture of patient data necessary to answer the study’s hypothesis. These patient data insights are then captured on specialized forms, called case report forms, that have been specially designed for the study. When participating in a study, medical professionals take on additional roles such as the Principal Investigator, Clinical Research Associate, and Clinical Research Coordinator, and perform the specialized processes associated with these roles.

In the last few decades, technology solutions, such as electronic data capture systems, trial management systems, and patient engagement platforms, have emerged to encourage greater efficiency in the conduct of clinical research.

While these technology solutions improve intra-study efficiencies, they don’t typically enable data reuse and interoperability across studies, healthcare systems, and stakeholders.

Medical professionals who are involved in research are often required to move between different technology systems, using separate workflows and often duplication of existing data into new systems. In addition, these solutions do little to address other factors complicating clinical research. In fact, it is possible to argue that some of the factors leading to costlier, slower results from clinical research are actually caused by technology. For example, digital innovation in healthcare is the driving force behind a surge in data access. Health-related data metrics are now being generated at an unprecedented rate, but the majority of those insights are normalized locally, making them very difficult to connect, combine, and share.

The patient experience is just as frustrating. For example, patients engaging in research are typically forced to move to an entirely different healthcare system with different physicians and ways of interacting with the medical system. Inconveniences like this are the consequence of trial designs that haven't evolved in decades. Figure 1 (below) shows the patient experience as they interact with two different systems upon entering clinical research.



**Figure 1:** Existing separation between clinical trials system and clinical care

Interventional clinical trials have long been considered the gold standard for clinical research, with good reason. Medical experts conduct trials which test a specific hypothesis, are rigorously controlled according to pre-defined criteria, and are engineered to eliminate or correct for biases. However, taking a broader view of clinical research within the context of industry-wide digital transformation, it becomes clear that reliance on this model presents some real challenges.

**These challenges include:**

- **“Trial specialist model”** limits the number of trials that can be conducted to the number of specialist roles in the clinical trials’ ecosystem. In fact, traditional trials are performed in a small percentage of all healthcare institutions worldwide.

- **High costs and relatively long timeframes are common** due to the level of rigor and regulatory oversight associated with traditional trials.
- **View of the patient’s overall healthcare journey is limited** to the data collected for individual studies.
- **Little interoperability, connectivity between studies, or reuse of the data** outside of the study, creating “research data silos.”
- **Challenges with patient recruitment and retention** because patients are often required to participate in a parallel environment to their normal clinical setting.
- **Strict inclusion requirements needed to accurately test a hypothesis are often not generalizable** to product use “in the wild”, where treatment in the trial may not reflect routine practice patterns, and the patients participating in the trial may not reflect the actual population that will be treated.
- **Data generated through healthcare digitization is largely untapped for research** despite the wealth of medical insights and data available as routine clinical service becomes digitized.

The challenges outlined above have driven some encouraging changes over the last few years. While interventional research remains a cornerstone for drug approval, regulatory agencies worldwide are beginning to require the use of data generated from real-world clinical practice to augment the results provided by clinical trials.<sup>5</sup> Industry and academia are beginning to use new study paradigms, such as pragmatic trials, observational studies, and considering hybrid trials, which combine multiple paradigms into a single study.

Despite these changes, data silos and lack of interoperability in today’s research operating model still make it difficult for researchers to incorporate real-world data, captured outside of the study into an interventional research protocol. Interventional research and real-world (observational) research today are distinct, not coordinated and in most cases are performed by completely different teams of researchers. While the results of one type of research may inform the other, current technologies and operating models do not yet allow the coordination and integration of these two types of research.

**Integrated research at the point of care**

From the expansion of telemedicine to use of wearable and mobile medical devices, changes in clinical practice are bringing life-saving treatments closer to the patient.

The results of these changes are often lower costs, greater convenience to the patient, and improved outcomes. However, today’s clinical research operating model has generally failed to adapt to this widespread healthcare digitization, focusing instead on improving individual study efficiencies.

The widespread adoption of EMR systems at the point of care provides an opportunity to reimagine the traditional clinical research model. Many of the problems outlined in the previous section can be solved by moving from a study-centric model to a “learning healthcare system”<sup>6</sup>, where the patient healthcare journey is electronically documented, organized, shared (appropriately and securely), and reused across multiple studies and stakeholders—both within and outside of life sciences. EMR platforms can be integrated with additional technologies and workflows to support clinical research. And with this integrated model, research becomes a natural output of the care process. Figure 2 (below) illustrates the new integrated model from the perspective of the patient.

<b>VISITS</b>	Point of Care (Physical or Virtual)
<b>SEES</b>	Research Clinicians
<b>WHO USES</b>	Integrated Research EMRs
<b>PRESCRIBES</b>	Researched Therapies, Procedures

Figure 2: Target system of integrated research

Specific benefits to an integrated research model include:

- **Research is moved away from a separate dedicated model**, enabling research to be performed through a network and platform that connects multiple stakeholders including providers, patients, and payers.
- **Research data silos are broken down**, enabling interventional and observational data to be included in the same research protocol.
- **The EMR creates a longitudinal record of real-world care delivery** providing foundation for the patient healthcare journey. Interventional study and other digital healthcare data can be linked to this journey to fill in and extend the record.

To fully optimize the value of this approach, it’s necessary to implement a complementary set of roles, processes and technology capabilities that reflect the new research operating model. One of the most significant changes will be reduced dependence on the specialized roles—such Clinical Research Coordinator or Clinical Research Associate—associated with clinical trials. Just as rideshare organizations like Uber and Lyft introduced technology-enabled drivers to replace the taxi driver and dispatch services, we envision a network of technology-enabled research clinicians serving as an alternative to the specialized roles associated with traditional clinical trials.

In addition, the regulatory framework will need to be modified to carefully manage the flow of patient data between routine care and consented research while protecting patient privacy.

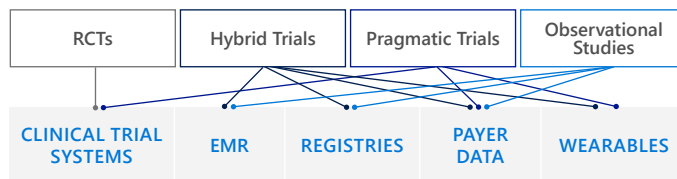
## Journey to the integrated research platform

A confluence of recent events—the digitization of healthcare, the widespread adoption of EMR systems at the point of care, and the increasing costs of clinical research—provide an opportunity for the life sciences industry to rethink and modernize the current research operating model.

Industry regulators have also taken notice. On December 13, 2016, the 21st Century Cures Act was signed into law to help accelerate product development and bring medical advances to patients who need them.<sup>7</sup> More recently, in July 2018, the U.S. Food and Drug Administration authored a new guidance document titled, “Use of Electronic Health Record Data in Clinical Investigations.”<sup>8</sup> The document encourages modernization of clinical research by leveraging new technologies and Electronic Health Records (EHRs). In December 2018, the FDA also released the “Framework for FDA’s Real-World Evidence Program,”<sup>9</sup> which describes the use of data captured through routine care delivery and supports the use of new indications for approved drugs and post-approval study requirements.

The shift to integrated research can occur gradually, allowing the use of specialized point solutions to decline over time as more capabilities emerge in the integrated EMR-based system and common regulatory challenges are solved. Ultimately, the integrated model allows researchers to conduct trials with the right mix of observational and interventional components, where traditional interventional studies are used only in those situations where they are necessary and appropriate. Ultimately, hybrid trials will become the new norm. Figure 3 (below) shows the As-Is and To-Be state, as the capabilities of the Integrated EMR-based Clinical Trials System become more complete.

### As-Is:



### To-Be:

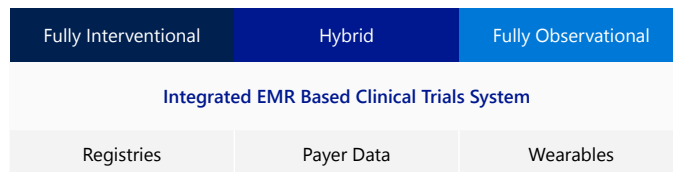


Figure 3: As-Is and To-Be state for clinical research

## Integrated research opportunities

The following is a partial list of opportunities for extending core EMR platforms with new technologies and capabilities to enable integrated research:

**Study feasibility:** A significant challenge associated with the current research model is the difficulty of accurately determining the feasibility of the trial design. In many cases, trials are beautifully designed to test the study objectives, but the sites and/or patients necessary to support the trial do not exist. In the current study-centric model, it's difficult to perform effective feasibility studies because data about patient characteristics, patient availability, site performance, and investigator availability are siloed and difficult to integrate. An integrated research platform inherently collects this data in one place, and can more fully enable effective and efficient feasibility studies.

**Digitized protocols:** The study protocol and related documents are some of the most important artifacts in a clinical trial. These data sources are often authored and managed as unstructured documents, resulting in inefficient manual review processes and challenges with quality control. In contrast, digitized protocols standardize key elements into a queryable format. The structured digital representations of a clinical trial streamline the review process and allow for detailed analysis of the relationship between trial design and conduct.

Digitization of trial protocols is particularly relevant in retrospective observational trials; the technology allows researchers to demonstrate that the protocols are not being manipulated after the fact to obtain a desired result.

**Protocol, patient, and physician match-making:** An EMR-based, integrated research platform can act as a “match-maker,” automatically identifying patients who qualify for study protocols. The system then alerts physicians of patients within their practice who qualify for research protocols, and enabling physicians to contact those patients electronically. There are many benefits to this type of protocol match-making, including the time-savings and efficiency provided by real-time analysis of patient data, and the ability to reach a broad group of patients and providers who are excluded from today's research operating model.

**Source data to populate case report forms (eSource):** One of the main strengths of traditional clinical research is the high quality of data collected—an aspect that also drives the high costs associated with clinical trials. While real-world data captured from routine care is typically of much lower quality, it is often much richer and deeper, providing additional information and context on the patient status. eSource initiatives seek to use technology such as AI and machine learning to curate RWE into high quality data for use in clinical research.

**Patient engagement:** Physician researchers can use patient engagement technology already integrated into many EMR systems (e.g. text messaging platforms) to reach out to patients who qualify for a study protocol and determine if they are interested in participating. If so, the same engagement platform can facilitate an electronic informed consent process.

**Extending EMR platforms to support research Electronic Data Capture (EDC):** Many studies require data that is not captured in real-world practice, including patient and physician surveys, patient diaries, and non-routine care. The current electronic data capture systems designed for clinical research are stand-alone systems. They are completely disconnected from EMR platforms that record routine care. With extended EMR systems that support research data capture, researchers can link the research data collected back to the patient data record.

**Virtual visits:** Current telemedicine capabilities provided in many EMR systems can be extended to support virtual study visits, allowing data to be captured without requiring the patient to travel to a study site.

**Creation of a “Digital Healthcare Journey”:** The use of the EMR as the foundation of research enables the creation of an integrated “digital healthcare journey” for each patient. Public EMR interoperability standards enable disparate digital healthcare data to be linked and connected to the appropriate places within the longitudinal patient record. Figure 4 (below) shows how each of these research opportunities can enable integrated research.

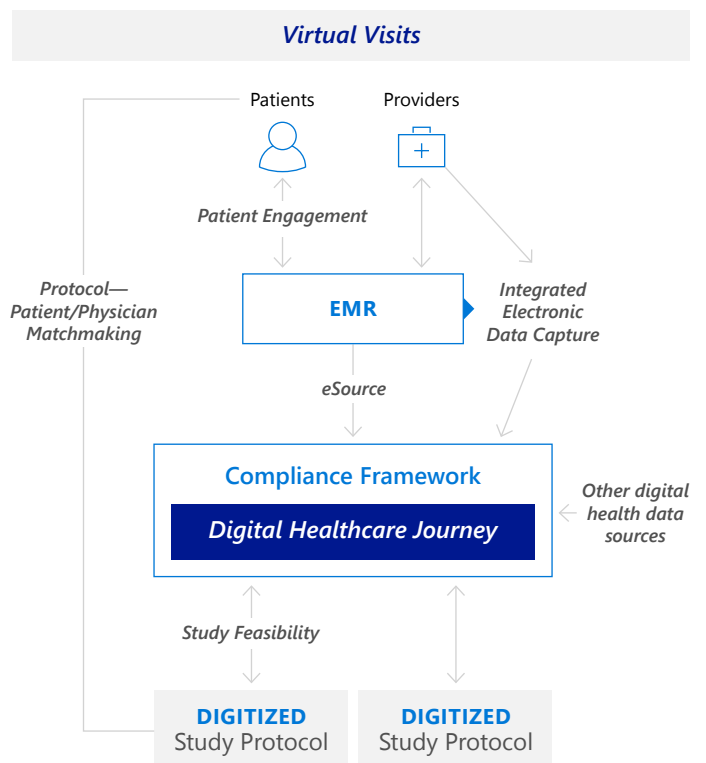


Figure 4: Extended EMR platform supporting integrated research

## Challenges of implementing an integrated research model<sup>10</sup>

While the EMR system's integrated approach offers a number of notable improvements, there are several important aspects to keep in mind as the system continues to develop and evolve.

In order to fully realize an integrated research model, medical researchers, decision makers, and leaders in the healthcare field should consider:

- Developing and implementing an appropriate regulatory framework
- Exploring and simplifying technical complexities associated with linking and integrating disparate data sources
- Proactively planning for the time and resources required to upgrade existing point-of-care systems to support the repeated use of high quality research data
- Modifying and implementing workflows to account for the new model's impact on long-standing, existing clinical workflows, roles, and processes

Addressing these focus areas will require collaboration across multiple stakeholders and disciplines—including physicians, regulatory bodies, policy makers, academics, patients and patient advisory groups, and electronic health record vendors and other technology vendors—in order for integrated research to successfully replace the current study operating model.

There are many groups and organizations currently working to advance relevant solutions to facilitate wider adoption of the integrated research model.

As noted earlier, the shift to an integrated research model can be implemented incrementally as modern strategies are developed and disseminated.

The current regulatory focus on the use of real-world data provides an immediate opportunity to implement this model for observational research. Once the relevant technologies and operational models have been used successfully in this capacity and the model becomes more mature, they can be extended further for interventional research.

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## Veradigm and Microsoft—committed to integrated research

Veradigm, a business unit within Allscripts, and Microsoft have partnered to fuel the healthcare industry's most forward-thinking strategies and innovative technologies.

Our partnership focuses on the implementation of a fully functional integrated research model, accelerating the study and discovery of life-saving treatments and clinical trials.

The collaboration will initially focus on extending Veradigm's cloud based EMR platforms, by integrating the solution with innovative, EMR-agnostic technologies that enable integrated research.

**Veradigm and Microsoft will also work together to develop pilot research programs to better understand, inform, and develop necessary processes, workflows, technologies and compliance frameworks to support research performed within this new operating model.**

## Conclusion

The advances in medical science over recent decades have been startling, yet the process of demonstrating the safety, efficacy, and patient value of new therapies and clinical practices remains inefficient. Some patients suffer unnecessary inconveniences when participating in trials, while other patients miss out on innovative treatments entirely, and many more are denied life-saving therapies for years.

By developing learning healthcare systems and integrating research into the point of care, we have the potential to lower costs, increase efficiencies, and remove bottlenecks that inhibit research—all while improving the welfare of patients. By removing data silos, a fully integrated research model has the potential to allow the blending of the best interventional and observational approaches. The barriers preventing this shift have largely been removed.

Now it's up to leaders, innovators, regulators and decision makers in healthcare to commit to developing the technologies, workflows, processes, and compliance frameworks to support a research model designed to enable, empower, and benefit research across the industry.

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In partnership with Microsoft, Veradigm is committed to a holistic approach to developing a learning healthcare platform that supports integrated clinical research.

The teams will work with the industry, providers, patients and regulators to ensure that the promise of this new approach is fully realized, bringing the practice of clinical research into the 21st century.

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