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Envisioning the site of the future

Integration of clinical research with clinical care driving change

By Karyn Korieth

The drug development world has been notoriously slow to adopt change, but industry leaders and visionaries expect the clinical research enterprise to change dramatically.

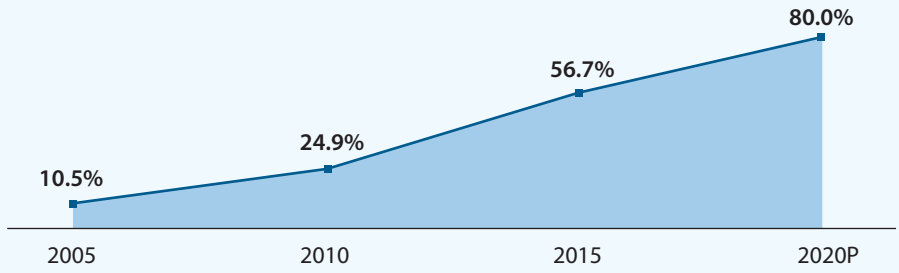
Integration of healthcare data, the power of data and analytics, a rapid move toward more targeted therapies and customized treatments, along with the desire for a lower cost R&D model are among the forces driving transformation in the way the research environment will function in the future.

As CenterWatch looks toward the decades ahead, we asked a team of experts, which included top-level executives and active investigators, to describe their vision of what clinical trials will look like in the year 2050. Many common elements emerged. The visionaries interviewed described a research environment where the traditional physical investigative site may not exist and one where clinical research and healthcare data become more integrated.

From drones delivering study drugs and the integration of clinical trials into clinical practices to roving teams of study staff, the scenarios predicted by our experts offer strategic insight for sponsors, CROs, investigative sites and other clinical research professionals.

Growth in EHR adoption

Percentage of office-based physicians with electronic health record systems



Source: Pew Research, 2016

Clinical research will follow the patient

Ken Getz, director of sponsored programs and associate professor, Center for the Study of Drug Development (CSDD), Tufts University School of Medicine, envisions a very different clinical research environment where patients are the central driver of where trials are conducted.

Based on ongoing research that we are conducting, as well as discussions with a number of experts and veteran clinical research professionals, we see a more flexible and transient clinical research environment supported by technologies and solutions that enable research to be conducted anywhere, at any time. In the future, clinical trials will be conducted wherever and whenever the patient wants to participate. It could be at the point of care or in the patient's own home or workplace through telemedicine and mobile technologies.

Another feature of the new clinical research enterprise is that it will be integrated into the broader healthcare environment. Clinical trial participation will be incorporated into the patient's routine healthcare activity. And clinical care will become more fluid and flexible through telemedicine as patients can speak with a professional and receive a diagnosis and care remotely.

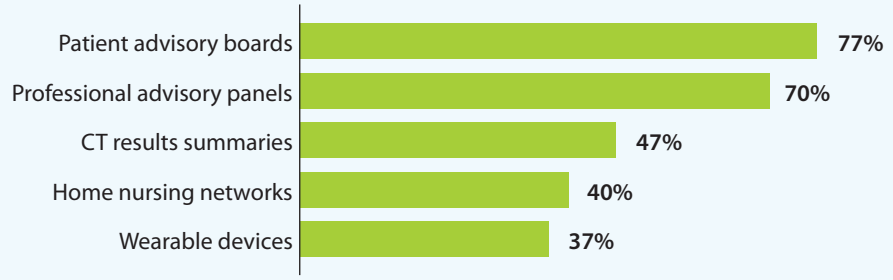
The clinical research team will be trained to be effective, roving professionals capable of quickly reviewing and analyzing massive amounts of data remotely and engaging with patients flexibly. In some instances, healthcare professionals may be automatically conscripted to serving as the principal investigator (PI), sub-PI or coordinator on the study. Healthcare providers will increasingly become key facilitators of study volunteer participation.

Today, clinical trials are conducted in fixed, physically distinct venues. They are typically isolated from clinical care and aren't supported by an engaged healthcare provider community. This new model gets rid of physical boundaries and puts patient engagement at the core, where it can become more fluid and where clinical research can be integrated into the continuum of clinical care.

As an integrated and integral community—patient, caregivers, healthcare providers and payers collectively collaborate with research professionals to define the most clinically meaningful and relevant study outcomes. Following commercialization, patient experience with newly approved therapies informs ongoing clinical care and future drug development planning and activity.

Top five patient-centric initiatives

Percent of total companies report piloting or implementing



Source: Tufts CSDD, 2016; n=30 companies; <csdd.tufts.edu>

Living rooms are the next clinical trial sites

Matthew Simmons, head of Drug Development at the Sarah Cannon Research Institute, part of HCA Healthcare UK, on how a siteless trial might look.

Just as we are moving to branchless banking or storeless shopping, siteless clinical research is a real possibility. Imagine a scenario where potential patients are identified through electronic medical record (EMR) searches with inclusion/exclusion criteria. They discuss the study and consent via a remote consultation with an artificial intelligence chatbot. Study materials are delivered to a patient—possibly by drone—and trial-specific apps pushed to the patient's smart device. Compliance is measured directly by smart pills. Live safety and efficacy data is streamed directly back to the EMR and then to the study database from wearable patches and personal blood analyzers.

Taking trials directly to the patient

Jennifer Byrne, founder and president of the Greater Gift Initiative and former chief executive officer of PMG Research, on the integration of clinical research into large healthcare systems.

By 2050, the vast majority of physicians will be employed by healthcare systems and we will have far fewer systems than we have today. Within these larger healthcare systems, research will become its own subspecialty. Research practice units will be baked in as part of large systems and physicians will specialize in research just as a neurologist or pulmonologist specializes. Today, clinical research centers within large systems are very decentralized and the researchers still work on a department level, but we are moving toward a much more sophisticated model of concentration and specialization where clinical research will be integrated into the system.

We are living in a world of electronic health records (EHRs) and we have a lot of other data, such as genomic sequencing data, behavioral health data, medical and family history and environmental risk. From a technology standpoint, we are going to have a platform that integrates that information. Because of the consolidation of the systems and the integrated technology, patients won't have to come to trials. Trials will come to patients. We will have the ability to pinpoint patients with unmet needs at precisely the time there is an alternative available and take clinical trial opportunities as an option directly to the patient.

The human element of clinical research will remain very important to the process. Research coordinators, as we know them today, will become research navigators. Their role, even in 2050, will be to provide that very high-touch relationship between the provider in the system and the patient. Whether we are talking 35 years from now or 100 years from now, a universal truth is that those relationships largely drive patient engagement in research opportunities. Machines can provide care, but there is a certain type of care that cannot be provided by a machine.

Investigators will become data scientists

Kathleen Griffin, executive director, Corporate Strategy at INC Research, on how technology will change the clinical research landscape.

The future is hard to predict because the rate of change is so fast now. Technology, along with the ability to access and mine data, is driving the change. It's not the other way around.

The role of study coordinators and investigators will be more about the data collected than about the face-to-face with the patients. They will become data scientists. You might have a primary PI with data and scientific knowledge to manage the data, and treating physicians would be sub-PIs. The primary PI would never see the patient, but instead deal with all the data being collected through routine visits or connected devices, either within the home or via smartphone.

As analytics and technology get smarter, we will learn more about science and medicine via mining data that is already out there, even predictively, so the shape of trials will change considerably. They will be smaller and more targeted. Sooner or later, we will be designing a drug for the individ-

ual. What does that kind of trial look like? Does it all happen via data? Potentially. We may get to a point where we don't need to do standard randomized, double-blind, triple-arm type trials, because we are collecting so much data from the real world.

Regulatory agencies are cautious. But they need to get on board and understand the technology and its ramifications on privacy and security in a much more rapid, continual fashion and not in a step-wise way. Those ramifications are never going to go away, nor should they. But we have to be quicker in our evaluation and determination about how to handle these issues because technology is moving us there, whether we want it to or not.

A future without clinical trial sites

Tomasz Sablinski, M.D., Ph.D., founder and chief executive officer of Transparency Life Sciences, on how telemedicine will drive change to the clinical trial model.

There isn't a question about what the clinical trial site will look like in 2050 because there will be no sites.

The purpose of clinical trials is to collect data from patients and generate interpretable data.

The most expeditious way of getting data is using direct communication between the patient's body and the database. Today, millions of patients stick a needle into their finger, drop blood onto a device attached to their smartphones and automatically share the results with a designated database, which might be a physician's hospital server. You don't need a site or third party. In five years, this will be possible with most physiological and pathological parameters. In 10 to 15 years, it will be possible with most everything we measure. In 30 years, chips implanted under our skin will measure physiological parameters 24/7 and the data will be transmitted to a computer, which could read it every second, or minute or hour. These will be your clinical trial visits.

Top five things patients like 'Least' about their clinical trial participation experience

Percent of total

30%	Not knowing whether I was getting the investigational treatment
22%	Location of the research center
19%	Study visits were too time consuming
16%	Compensation was not enough given the demands of the study
15%	Study procedures were too cumbersome

Source: CISCRP, 2015; n=12,009 global respondents

In 30 years, I don't see any future for a physical site, except for those trials where surgery or invasive procedures are involved or something like an MRI or IV is needed, although I could even be wrong about that. You can already do a very high-quality ultrasound by a device that attaches to your tablet, and the technology to deliver proteins and peptides is advancing rapidly.

The way clinical trials are done reflects medical practice. Today, medicine is practiced mostly by interface between the physician and patient. For most decisions, the physician doesn't need to see the patient. Telemedicine will force a huge cultural and communication shift in healthcare. It's safe and cost-conscious. Payers will push innovation to healthcare and they will refuse to pay bills for anything that doesn't clearly add value. Clinical trials will have to follow suit.

The promise of real-world evidence

Jeremy Gilbert, vice president of Product Strategy and Development at PatientsLikeMe, on the evolution of a learning healthcare system in which data from clinical practice and scientific investigation converges.

As the cost of clinical trials continues to rise and the size of potential markets shrink, it's inevitable that people will rethink this institution. It won't mean just introducing the latest wearable, but a move to a learning healthcare system.

If you have been diagnosed with rheumatoid arthritis and ask a rheumatologist to recommend treatments, your doctor doesn't know what is going to work for you and will make a guess. In that moment, they are doing an experiment on you. The only difference between that and a pragmatic base for a clinical trial is that in the case of the rheumatologist and the patient meeting in the doctor's office, the results of the experiment are never recorded and there is no protocol for what they did.

We are going to see a convergence point where doctors pull as much evidence as they can about a patient's molecular subtype, preferences and history, and about the journey of many other patients to inform their treatment decisions. That same data set then becomes equally useful for understanding the efficacy and safety of new medications. In that world, companies submit to the FDA based on initial safety and phase I studies, but much of the evidence generated comes from the real world through some form of conditional use being monitored by this network.

When you go to your doctor in 2050, you will be molecularly profiled. The sub-type of your disease will be known and it will be computer-matched. It is already happening in oncology. The system will run a simulation of your biology against the known therapeutic agents for your condition. Maybe it will find that the best drug for you has not been approved yet. In that case, the doctor will say, "I'm not an investigator on this clinical trial, but if I submit my application right away, I could become

one and we could do this work together and submit it." It's much more of an on-demand, fluid type of process.

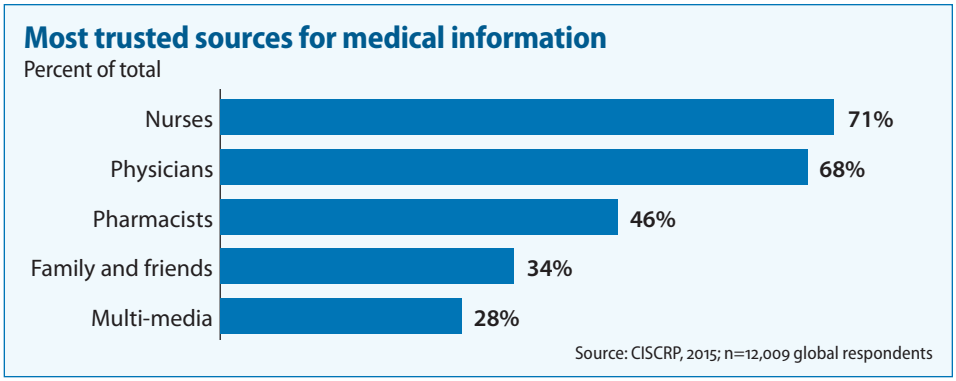
In some cases, the government might want to see a randomized controlled trial (RCT) due to the risk-benefit profile of a particular molecule. Traditional trial structures will be used in those cases. For safety trials, until our understanding of biology becomes better, we are probably going to see at least initial phase I safety trials simply because someone has to be the first to try a molecule, and ethically, it's hard to imagine that not happening in a very controlled environment. But the model of running a pivotal RCT before getting on the market can't continue. We can't have precision medicine and a value-based healthcare systems, which is what we are rapidly moving to both in the U.S. and ex-U.S., and have expensive clinical trials. There will be other rich and much more pragmatic information sources that can be used for evidence generation.

Site workforce will shrink

Ana Marquez, CEO of Clinical Site Partners in Miami, Florida, on the downside of a virtual clinical trial model for today's investigative sites.

As machines become more sophisticated and robots take on a greater role, there will be fewer people involved in clinical trials from a site's perspective. I can foresee electrocardiograms (ECGs), for example, which are now conducted at the sites, being done in subjects' homes by the subjects themselves. PIs will be doing fewer procedures in-house and, instead, have a more supportive role, one where they guide patients and answer questions. It will be harder for sites to be profitable and we may see a decline in physician participation.

Physicians have tremendous influence over a subject's participation in a clinical trial. As site involvement decreases and trials take on a more virtual role, the public's trust in the clinical trial process may decline as research will become a far less personal experience.



Fewer trials and more convenient site locations

Lindsay McNair, M.D., chief medical officer, WIRB-Copernicus Group (WCG), on the potential impacts of big data and patient centricity.

We will be doing fewer clinical trials in 2050 because the promise of big data will be closer to reality. We will be able to answer a lot more questions by looking at data that we have already collected since the data sets will be richer, better integrated and more useful in terms of answering questions. We may not need to do as many prospective studies when we can answer questions with retrospective data.

The movement toward a patient-centric model of drug development will drive organizations to look at a variety of settings where people can participate in research. There will be more study site locations, so that people don't have to drive to an academic medical center, and participants will be able to pick up study medications at their local pharmacy rather than going to a research pharmacy. We will think more about the convenience of the participants and how that carries over into recruitment and retention.

There are some areas where we will see a lot of change and other areas where we won't see much change at all. The model of a controlled clinical trial will not fundamentally change. Having a scientifically valid, controlled experiment to determine whether a new product is better than an existing treatment will still be with us in 30 years.

New ideas about data privacy

Raffaella Hart, vice president of Institutional Review Board (IRB) and Institutional Biosafety Committee (IBC) Services at the Biomedical Research Alliance of New York (BRANY), on how patient attitudes about data sharing and privacy concerns will advance to improve healthcare outcomes and clinical research.

Our ideas about what health information is okay to share for research purposes and how much consent we need to give will evolve, and will have to evolve. To do health outcomes research, we need to have more publically available data or more easily accessible de-identified data.

The concept of a learning healthcare system will change cultural expectations. There will be different models of consent. People could have an expectation of wanting their doctor to use the knowledge gained in their evaluations to improve their healthcare, their family's healthcare and everybody's healthcare in the future. They wouldn't necessarily have to sign a consent form to contribute at every visit.

New skills needed for study staff

Jim Kremidas, executive director at the Association of Clinical Research Profession-

als (ACRP), on the evolving roles in clinical research.

By 2050, clinical research will be integrated into the typical clinical practice arena.

Data from EMRs based on patients' normal clinical interaction with their doctors and information collected during study visits will eventually converge. The amount of data about patients that will be captured will open all types of opportunities to do research that doesn't necessarily involve too much intervention with the patient. As we get more data and can see what the best treatment algorithm is with existing treatments, it would be relatively easy to drop in a new therapy that is in development and see how those patients do compared to people who aren't even in the trial. Your control group becomes the standard of treatment and all that data that is already being collected.

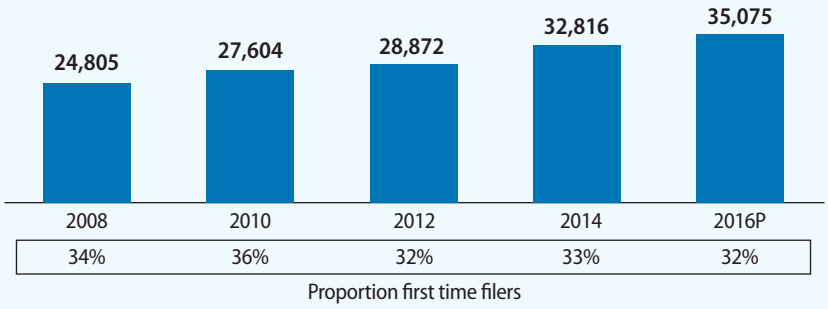
For this vision to come to fruition, technology and the way data is captured both in the normal clinical setting and the clinical trial setting need to be standardized. Processes also need to be standardized. How do you conduct a trial in the real-world setting? The third piece of the equation is the professionals conducting the research. How do you standardize and train to make sure people have a certain level of competency to conduct a trial?

Roles in clinical research will continue to evolve based on new technologies and processes and consequently, people need to be prepared for that evolution. The study coordinator role is already starting to morph into subspecialties and CRAs are becoming problem-solving relationship managers as opposed to auditors.

Patient participation in research increases

Mohammad Millwala, chief executive officer of DM Clinical Research in Tomball, Texas, on the evolution of physician investigators.

A fragmented global community of FDA-regulated investigators



Source: Tufts CSDD; <csdd.tufts.edu>

In the age of driverless cars in the sky and advanced augmented reality, subjects interested in research will consent online and a virtual clinical research coordinator will do the entire study visit wherever the patient is. Hence, if various regulatory agencies move forward with technology, there will be global trials conducted from a central operating center. The PI will be the main doctor in the central operating center—similar to a command center—overseeing information and safety data collected in electronic health records.

The level of awareness about clinical trials will multiply as each and every doctor will be trained to educate their patients for research. It will become part of normal healthcare and, hence, we will see huge participation. A specialized workforce will be required to keep up with the sheer volume of patients participating in research. Additionally, since research protocols will be designed to include flexibility for each individual patient, the workforce will need to manage more complex, but more effective, protocols.

Patients review study ethics

Kimberly Irvine, executive vice president and chief operating officer of BRANY, on building trust in the future research enterprise.

From an IRB perspective, regulatory changes might require that the composition of ethics boards or IRBs include members who focus on data privacy. Today there are requirements for scientific and non-scientific members. But perhaps there would be requirements to have data privacy experts or an actual patient on the committee to ensure that all aspects are considered for clinical trials of the future. You might need this in order to give people some sense of trust that the research is being reviewed by all of the right experts.

If research was more transparent to patients, maybe the level of distrust we have today will have subsided because we've put mechanisms in place to share more of our results and people are more confident in the research process. If we want people to become more accepting about the use of their information for the good of humanity, they need to feel more empowered and trusting of the use of that information.

Clinical trials become a routine care option

Lucas Litewka, director of the University of the Sunshine Coast's Clinical Trials Centre in Sippy Downs, Australia, on the potential for integrating clinical trials into medical practice.

Consumers will have greater control about healthcare choices and access to the full-spectrum of treatment options, of which clinical trials will be a key part. I can imagine a growing consumer appetite for participating in trials and demanding access to novel treatments without delays. An essential element of choice for patients will include greater access to avail-

able empirical evidence about their health condition and the treatments being offered. As a result, recruitment methods will be vastly different from what we do today. Similarly, clinical trials themselves will become more mainstream and be seamlessly integrated into everyday medical practice.

Continuing need for science-driven experiments

Frank Rockhold, Ph.D., professor of Biostatistics and Bioinformatics, Duke Clinical Research Institute, Duke University School of Medicine, on how clinical trials in the future shouldn't change.

We are doing a pragmatic randomized clinical trial (PCT) for aspirin with 20,000 patients where there isn't a classic site. The patient may go to see their healthcare practitioner, but the doctor is not an investigator. The primary data collection mechanism isn't even the EHR. Patients self-consent, self-randomize and report data through an online portal. The whole study is derived from patients. The investigative site, as well as traditional trials, almost disappear in the model.

There is a difference, however, between doing a trial like this in an approved drug versus a non-approved drug. Our pragmatic trial model is around a marketed product, which has a label, and there is a system in place to report spontaneous events. For unapproved drugs, you have to go back to something closer to the current model. Even the learning healthcare system can't help with a drug that isn't marketed. Although there are exceptions, particularly in cancer treatments, in general, there aren't a lot of unapproved drugs listed in EHRs.

Big data has its uses in figuring out how the data that is in healthcare systems can be used to improve how to identify patients, target care and get information to practitioners. Study designs for comparative effectiveness or how treatments are used will change and evolve. But that is not the same as doing an experiment to determine whether something works or not. They are both important, but for the foreseeable future, one doesn't replace the other because we are answering different questions. If we stop doing experiments to evaluate new medical therapies, that is a step backwards.

Implications for today

These glimpses of the future landscape offer stakeholders throughout the research enterprise a vision of how thinking needs to evolve going forward. While some of the new approaches may be dismissed as too radical, steps toward many of these changes have already begun. The scenarios raise many questions, including how research integrity, data quality and patient privacy will be maintained in future models and how quickly the transformations will happen. Yet radical changes in the landscape are considered inevitable.

"If we keep thinking about solving issues in just small ways, we are losing opportunities," said the Greater Gift Initiative's Byrne. "Necessity is the mother of invention. You can only say we are on a cross-course for disaster for so long before you have to start thinking out of the box and moving to a different sort of action. Everybody in this field has a responsibility to be thinking ahead and to how it might be different. We need to be thinking that we are part of the future."

Karyn Korieth has been covering the clinical trials industry for CenterWatch since 2003. Her 30-year journalism career includes work in local news, the healthcare industry and national magazines. Karyn holds a Master of Science degree from the Columbia University Graduate School of Journalism. Email karyn.korieth@centerwatch.com.