Clinical Researcher

The Authority in Ethical, Responsible Clinical Research

April 2021 (Volume 35, Issue 3)

Diversity, Equity, and Inclusion in Clinical Research? We Can Do It!

Clinical Researcher—April 2021 (Volume 35, Issue 3)

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EXECUTIVE DIRECTOR'S MESSAGE

Reaching Out Will Lift Us All

Jim Kremidas

Tuskegee. Henrietta Lacks. Project MKUltra. These and other names associated with reprehensible blemishes in medical research history continue to haunt us today. As COVID-19 has reaffirmed, a disproportional high percentage of African Americans and some other underserved groups remain wary of participating in clinical trials—either as patients or practitioners—in part due to certain rare, but sadly infamous, situations. It's time we as an industry did more to work with those who are skeptical about our mission and its purpose.

Elsewhere in the pages of this issue, ACRP Association Board of Trustees Chair Erika Stevens lauds the work of our new Diversity Advisory Council (DAC). I share her enthusiasm for the people on the DAC who have come together to advance diversity in both the clinical trial patient and workforce populations. The DAC is on the verge of some exciting announcements about some game-changing initiatives. Watch this space for more on that.

However, I'd like to focus this month on ACRP's innovative and expanding Find Your Element campaign. As you know, the demand for clinical trials is growing faster than the pool of clinical research professionals, threatening the quality of trials and undermining attempts to bring more innovative treatments and therapies to vulnerable patients.

Thanks to the support of the ACRP Partners in Workforce Advancement, the Association launched Find Your Element to help raise awareness of the clinical research profession among college students. We are devoting a special emphasis on two- and four-year colleges with traditionally high percentages of minority student populations.

Put simply, we and many others believe a key to promoting greater participation among all groups in clinical trials is to further diversity the actual clinical trial workforce. It's widely accepted that most people learn about clinical trials from their healthcare practitioners. If we are serious about restoring trust with underserved populations, we must do a better job of recruiting and retraining a more representative workforce in our industry.

The team at ACRP is honored to help industry achieve this shared goal of greater diversity. If you'd like to volunteer your efforts in this worthy cause, we'd love to hear from you. Please feel free to reach out to me at jkremidas@acrpnet.org.

Jim Kremidas is Executive Director of ACRP.

CHAIR'S MESSAGE

Diversity in the Clinical Research Industry

Erika Stevens, MA

Does the clinical research industry support diversity?

While the U.S. Public Health Service has mandated generalizability of clinical research across populations since the late 1990s,{1} an increased recent emphasis on diversity has emerged. The 21st Century Cures Act{2} provides support for the advancement of clinical trials, while enabling increased funding and removing barriers to accelerate research. Following the release of legislation, the National Institutes of Health (NIH) issued a policy amendment encouraging the inclusion of women and minorities in trials.{3} The revision requires valid analysis and reporting of sex/gender, race, and ethnicity through ClinicalTrials.gov.

Later, the NIH released several requests for proposals which encouraged the inclusive representation of diverse populations in clinical research. In the fall of 2020, the U.S. Food and Drug Administration issued a guidance for industry on enhancing diversity in clinical trial populations.{4}

However, little emphasis on diversity in the workforce is evidenced in the clinical research industry. The NIH published a notice of interest in diversity among researchers in the research and discovery process.{5} The notice focuses on scientists and trainees with diverse backgrounds, but does not address the clinical research workforce.

ACRP is leading the way in raising awareness of diversity in the workforce, having recently launched a Diversity Advisory Council (DAC). This resource provides strategies for recruitment and retention of clinical research professionals from underrepresented groups, and is charged

with creating a culture of inclusive excellence for the clinical research and life science community. The goals of the DAC are to grow the diversity of the workforce; develop and enrich the existing minority workforce; and improve organizational effectiveness and engagement on the value of diversity, equity, and inclusion. To meet these objectives, ACRP's DAC is raising awareness of clinical research as a career at colleges and universities, offering mentoring opportunities, and developing thought leadership collateral.

Among these initiatives are those aimed at increasing clinical research course offerings, enabling employer connections, and conducting a baseline survey assessing current demographics. We also need to work toward establishing greater awareness of the importance of attracting more bright and diverse minds to our enterprise early throughout the industry.

ACRP continues to be a leader committed to increasing diversity in the clinical research workforce. As Chair of the Association Board of Trustees, I am excited to support these initiatives to expand diversity of the clinical research industry.

I wish you all the best jusqu'a la prochaine fois (until the next time),

References

1. https://www.govinfo.gov/content/pkg/USCODE-2011-title42/pdf/USCODE-2011-title42-chap6A-subchapIII-partH-sec289a-2.pdf
2. https://www.govinfo.gov/content/pkg/PLAW-114publ255/pdf/PLAW-114publ255.pdf
3. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-014.html
4. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial
5. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-031.html

Erika Stevens, MA, is the 2021 Chair of the Association Board of Trustees for ACRP and leads Transformation Advisory Solutions for Recherche Transformation Rapide.

A Clinical Research Center's Story of Change and Adaptability During COVID-19

Holly Bookless, BSN, RN, NE-BC; Paula Smailes, DNP, RN, CCRP; Todd Lusch, BA; Deanna Golden-Kreutz, PhD

What was originally known as the extramural General Clinical Research Center (GCRC) program was funded from the 1960s, first by the National Center for Research Resources within the National Institutes of Health (NIH), and then as part of the Clinical and Translational Science Awards (CTSA) program via NIH's National Center for Advancing Translational Sciences up until about seven years ago.{1} While the NIH-backed funding dynamic has changed over the years and the GCRC itself has been defunded, NIH CTSA support to academic medical centers (AMCs) has had a lasting impact. With or without current CTSA funding, integral programs at AMCs across the United States continue to yield successful research thanks to infrastructure created with federal help for facilitating studies that may be otherwise challenging for investigators to complete.

The Clinical Research Center facility (hereafter referred to as "the center" in most cases) at The Ohio State University Wexner Medical Center (OSUWMC) is now based within the College of Medicine's Center for Clinical Research Management and includes 11 beds, a metabolic kitchen, a processing lab for biological samples, and an analytical and development lab for assays.{2} The center's staff consists of a nurse manager, a fiscal officer, two clinical research coordinators,

six nurses, a registered dietitian, two clinical research assistants, and three research lab technologists. These resources currently support 130 active protocols and involve more than 2,500 participant visits per year. Studies span multiple therapeutic areas in Phases I through IV for both inpatient and outpatient settings. While the predominant hours are 7 a.m. to 5 p.m. Monday through Friday, 24/7 care can be provided when necessary for inpatient participant studies.

COVID-19 Impact on Business Operations

While the normal, busy operations of the center were occurring a year ago, the threat of COVID-19 came to fruition when the Governor of Ohio announced on March 12, 2020 that the state would be shutting down many operations to help prevent the spread of COVID-19. With that, research leadership began determining which research studies would continue versus those that should temporarily stop. It was decided that only therapeutic trials would be continued. While most studies did well shutting down, concern did exist for some investigators with respect to study and funding timelines.

The Clinical Research Center at OSUWMC, with which all the authors of this article are engaged, remained open and continued research activity. Because of this, we were able to help with studies that did not otherwise have available research staff.

Alternative Work Arrangements

With a reduction in workloads, initiatives were created to keep staff off campus when possible. Some center staff transitioned to work from home and needed assistance with resources, which included setting up equipment and network access. Guidance from research leaders was provided for what activities would be appropriate to do from home. When applicable, staff were assigned work that did not involve direct participant care, such as data entry, standard operating procedure development, equipment ordering/inventory, and professional development.

One particular concern related to the possibility of COVID-19 exposure for the center's staff and participants, along with the possibility of transmission. Therefore, staff were also assigned to develop safety workflows to mitigate COVID-19 risk when working at the center.

Supporting the Health System

Space

As with most AMCs, space is a hot commodity at OSUWMC. As a result, the medical center conducted an assessment of space to determine what areas could be used for a possible rise in COVID-19 admitted patients, including use of the Clinical Research Center. With a possible upsurge of COVID-19-positive patients, leadership determined that the center could possibly house COVID-19-positive patients or formerly positive patients awaiting a second negative swab.

The building that houses the center also includes the medical center's rehabilitation hospital. The rehabilitation hospital began to have space issues related to the need to keep patients in private rooms for proper distancing; for this reason, patients were moved into open beds located in the center. Research supplies and equipment had to be moved and stored in office spaces and other rooms to accommodate the rehabilitation patients moving in temporarily. Rehabilitation patients without COVID-19 were sent to the center and occupied nine beds. Since rehabilitation nursing is a specialty area, the associated nursing staff followed these patients to care for them on our unit.

The center housed the rehabilitation patients from the end of April until July 2020. In mid-July, the center returned to normal operations; however, in mid-August the rehabilitation patients returned due to space issues. This time, the move was simplified by sharing some supplies, while keeping important billable and research supplies separated. As a result, "research only" space for staff and research equipment was created. The ultimate configuration of the center during this time and currently is that COVID-19-positive participants are on one end of the unit (three beds), COVID-19-negative research participants on the opposite end (three beds), and medical/surgical patients from University Hospital in the middle (six beds, with three being semi-private). Specialty equipment for the center had to be moved out and is being stored until normal operations resume.

Staff

While the center's operations were being revised, a plan for redeployment of staff to other areas of the medical center began in response to the potential increase in hospital occupancy due to inpatient and critically ill COVID-19 patients. Five of the six existing nursing staff were identified for potential deployment to assist with a potential COVID-19 surge. In preparation, these nurses underwent specialized training for the electronic medical record and general patient care; this included possible deployment to intensive care units, depending on nursing experience. To date, there has been no need to deploy center staff to other units. Hospital and research leadership determined that research staff would be one of the last groups to be deployed due to their critical role with forwarding the research mission, including the conduct of important therapeutic COVID-19 studies at our AMC.

Conducting COVID-19 Research

When the majority of the world was closed due to the emerging pandemic, the Clinical Research Center needed to continue supporting the medical center's activity of direct patient care through research while also developing processes to manage the impact of the COVID-19 virus. Initially, the center began working on several studies related to exposures to COVID-19 and frontline healthcare workers. Overall, the center completed close to 1,300 visits with healthcare workers from May to July 2020. This experience prepared the team to move forward quickly when the College of Medicine's Office of Research approved a restart of both non-COVID-19 and COVID-19-positive studies in July 2020.

The first study was for those with mild to moderate COVID-19 symptoms for an outpatient monoclonal antibody study. This study required participants to be onsite at the center. At the same time, COVID-19 vaccination research was preparing to start. This research required the center to complete visits if the participant became ill after being vaccinated.

Challenges and Solutions

These studies necessitated consideration regarding the logistics of COVID-19-positive and COVID-19 high-risk participant movement and samples. A COVID-19 Clinical Care Committee reviewed the research protocols allowing COVID-19-positive participant studies at the center. As part of the review process, an epidemiologist walked through the unit with the study team, principal investigator, and the center staff. Questions arose about processes that needed to be developed, including the following:

- What building entrance should be used for COVID-19-positive participants?
- Where should personal protective equipment (PPE) be sourced in order to not interfere with clinical needs for PPE?
- How do we complete procedures and handle samples safely with COVID-19-positive participants?
- How do we lessen our staff's exposure and decrease their overall time at the bedside with COVID-19-positive participants?
- How can we lessen the risk for COVID-19-negative inpatients and non-COVID-19 research participants on the unit while completing COVID-19-positive studies?
- How will the rooms be cleaned after COVID-19-positive participants leave?

To answer the questions about these challenges, solutions were created (see Table 1). To execute COVID-19-positive studies, the study sponsor or sponsoring department purchased PPE and other necessary supplies. N100 masks and replacement filters were supplied by our organization. Special training for proper donning and doffing of PPE was reviewed with staff as provided by the medical center. Hand hygiene was stressed, with hand sanitizer dispensers being located in all patient rooms and outside all patient doors. Institutional hand hygiene policy requires nurses to clean hands upon entry and again when leaving patient rooms, after touching any surfaces, and prior to and after gloving and/or any patient contact.

Table 1: Challenges and Solutions During the Pandemic

Challenge	Solution(s)
Shortage obtaining supplies/PPE	• Ask sponsor to provide first, then organization.
COVID-19 patient logistics	• Consult epidemiology for staff workflows and participant activity. • Develop guidance for unit activity and participant safety.
Staff working from home	• Assign remote duties such as data entry, policy development, and computer-based learnings for professional development. • Provide computers and monitors and ensure connectivity.
Study teams and center staff fears and concerns for COVID-19 transmission	• Provide emotional support. • Provide education related to safe COVID-19 practices. • Refer to employee assistance program for mental health services.
COVID-19-positive patient exposure time	• Communicate through the Updox system and conduct virtual participant monitoring. • Conduct continuous assessment of processes and support to adjust procedures quickly as needed.
Research participant safety and prevention of COVID-19 transmission	• Cluster COVID-19-positive participants away from non-COVID-19-positive participants. • Terminally clean rooms after use. • Use PPE and established hand hygiene practices.

Collaboration to reopen research activities was done with the following support areas:

- The Clinical Research Center Registered Dietitian worked with the Respiratory Therapy and Epidemiology Departments to understand metabolic cart equipment operation and cleaning after use for COVID-19-positive participants, which is designed to perform indirect calorimetry, oxygen consumption, and exhaled CO_2 tests.
- Epidemiology was consulted for ongoing review of procedures to ensure processes were safe.
- Respiratory therapists were involved in spirometry and exercise studies so that their input could be gained into the safe operation and cleaning of equipment during the pandemic.

COVID-19-Positive Study Participants in the Center

COVID-19-positive study participants were screened prior to arrival at the center to ensure eligibility. If during the recruitment process it was determined that a participant did not qualify, they did not come to the unit and were advised to follow up with their primary care physician. However, upon arrival eligibility was again reviewed; participants could potentially be screen failures once at the unit due to unstable vital signs. For COVID-19-positive participants coming to the center, a workflow was developed to ensure safety for staff and patients (see Figure 1).

Figure 1: COVID-19-Positive Participant Workflow in the Clinical Research Center

Patient arrives and phones unit. → Staff don PPE and meet patient at their car. → Patient given surgical mask and hand sanitizer. → Second staff member clears hallways, opens all doors, and pushes all elevator buttons. → Patient escorted to Clinical Research Center via back entrance. → Patient taken to room and vital signs taken. → Eligibility review and virtual monitoring set up from participant room to nurses' station. → Patient education for virtual study procedures. → Study procedures executed with virtual monitoring. → Study visit complete. Patient discharged. → Paient escorted off unit the same way they entered the unit/building. → Room terminally cleaned and UV treated per environmental services.

COVID-19-Positive Participant Arrival

After the COVID-19-positive participant parks their car, the participant calls the center nurses' station to notify staff of their arrival and the assigned number of their specific parking spot. The participant would remain in their car while CRC nurses donned the proper PPE including N100 mask, hair cover, face shield, gown, and gloves. The nurses would meet the participant at their car with hand sanitizer, a surgical face mask for the participant to wear, and an ID band to identify the participant.

The participant was not permitted to touch anything, including the door, elevator button, etc. In some cases, they would be taken by wheelchair to the unit. Participants and staff would enter the back side of the unit away from the nurses' station and most other unit activity. Another staff member would help with opening doors, using their badge for entry, and clearing the hallway of patients and staff.

There was a commitment to having strong communication with other staff working in the building, so they were aware of what was occurring. Height and weight were collected on the way to the room on a designated scale. These participants had mild to moderate symptoms and only a few participants had any shortness of breath or cough.

Study Execution

Once the research participant was in a center room, vital signs, pulse oximetry, and a general medical/surgical history were collected. Virtual monitoring was done with the utilization of Updox to reduce staff exposure time with the COVID-19-positive participant. (Updox is a Health Insurance Portability and Accountability Act–compliant, web-based communications platform using video to interact with patients virtually.)

A study doctor would perform the physical and ensure participant eligibility before nurses started their research care. Once the participant qualified, the center nurse worked with the participant to do urine pregnancy testing (if applicable), IV placement for blood work, vital signs, and review of surgical, medical history, current medications, and allergies. The nurse also completed a nasal

swab and saliva sampling for the COVID-19-positive diagnosis and, most importantly, ensured the participant is comfortable.

For ongoing monitoring, a laptop was placed in participant's room and a second laptop was placed at a desk near the telemetry monitoring system. The link to Updox is sent to the nurse caring for participant. The center staff member opens the link on the laptop in the room and ensures video and sound are enabled. Another staff member or nurse stationed near the telemetry machine ensured the participant was visible, including the ability to see chest rises for respiration monitoring, face, and IV medication pump reading.

Staff donned and doffed PPE several times depending on study activities per medical center policy. Virtual monitoring helped to reduce the amount of PPE used and lessened staff exposure, thus promoting safety.

For studies with investigational IV medication administration, the nurse caring for the participant does as many activities as possible pre-infusion/medication administration. The nurse also ensures a good visual is in place from the desk via the laptop in the participant's room. The participant is instructed on how and when to take their temperature when blood pressure monitoring is completed. Pulse oximetry measurement is checked continuously and this can be seen virtually at the nurse station.

A staff member located at the center's nurse station checks respirations, heart rate, and blood pressure every 15 minutes and continuously monitors the participant during infusions to ensure there are no issues with tolerance and side effects. The nurse caring for the participant must re-enter the room when investigational medication is ready per pharmacy and leaves the room so virtual monitoring can be done at the desk.

COVID-19 Study Samples

Samples are sent to the analytical and development lab for processing within the Biosafety Cabinet. For nasal swabs, once the specimen is in the medium, it is believed to no longer pose a threat of exposure to staff; however, it is still handled per lab safety standards and required PPE. The swab is placed in a biohazard bag and is wiped with a disinfecting wipe. A second biohazard

bag is placed over the first biohazard bag and is also wiped. Glove changes and hand washing occur before and after each bag is applied. Swabs are delivered to the lab and they are labelled as COVID-19-positive, packaged, frozen, and shipped.

Patient Discharge

Per consult with epidemiology, Sani-wipes® are used by the nurses upon discharge to effectively kill COVID-19 on surfaces and provided by the institution for this purpose. After COVID-19-positive patients are discharged, the room is terminally cleaned and UV-treated per environmental services and institutional policy.

Support for Non-COVID-19 Studies

COVID-19 research was being conducted at the same time as non-COVID-19 studies. Staff members were given a rotation of work assignments (concentrating on non-COVID-19-positive assignments on some days and focus on COVID-19-positive assignments on others) and highlighting and celebrating when goals such as a top recruiting site and/or the first site to enroll a participant were achieved.

Discussions occurred with individual research teams and lead center staff regarding the safety and plans to minimize exposure to COVID-19 for participants and research staff. The center's nurse manager oversaw these discussions while the staff nurses would review the revised center processes and provide insight on institutional rules and policies.

Study teams were asked to do COVID-19 pre-screening on all participants. Participants were met outside due to the locked doors of the center building. Participants were required to wear surgical masks provided by the study team. Masks were essential and had to be worn by the participant for the entire research visit despite the length of the study visit. Some visits could last for 10 to 12 hours, and education was provided to the participant prior to study visits regarding the need to wear a mask the entire visit.

The New Normal

As we continue to work toward routine research operations, the COVID-19 pandemic promises to bring more barriers to the conduct of clinical research. However, overcoming challenges and capitalizing on the solutions we've developed will hopefully allow the Clinical Research Center to be better prepared in the future. At the same time, potential new options for the growth of research operations exist with tele-research visits, electronic and virtual consenting, and other virtual research activities.

Many future opportunities to study and learn about COVID-19 are inevitable. The processes and procedures the center has in place, including support from research leaders, essential open communication, participant safety, and teamwork among staff, will sustain the operations of our center for both COVID-19-positive and COVID-19-negative studies. This promises to promote the research enterprise at our organization and beyond.

References

1. Nathan DG, Nathan DM. 2016. Eulogy of a Clinical Research Center. *J Clin Invest* 126(7):2388–91. doi:10.1172/JCI88381. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4922700/#:~:text=The%20first%20extramural%20GCRC%20grants,and%20therapeutics%20in%20volunteer%20patients
2. https://ccts.osu.edu/content/clinical-research-support

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PEER REVIEWED

Fixing the Foundation: Applying Digital Strategy and Process Automation to Manage Business Functions in Clinical Research

Christina Morris; Erika Stevens, MA

Biotechnology, medical device, and pharmaceutical companies are seeking other industries' disruptive digital technologies to aid in improving operational efficiencies and resourcing. For example, customer-centric robotic process automation (RPA) is thriving as an approach to handling routine financial processes in information technology, warehouse management, customer service, and healthcare areas,{1} and its wider applications have attracted interest from more research-oriented sectors.

Think about your all-in-one banking app; through the user interface, the customer is delivered the content or data they need, when needed. The user interface and the desired end-user (customer) experience (outcome of the interaction) are usually orchestrated by a digital process application that is integrating and/or connecting with other applications or data sources. The data orchestration manages the data, and the user interface manages the end-users' desired experiences (see Figure 1).

Figure 1: Conceptualizing the User Experience, User Interface, and Customer Experience

User Experience (UX)

Think of the User Experience (UX) as the plans for a building. The blueprint doesn't say how the building will look, like paint color, but it does tell the entire team how it is to be built to meet a user's needs.

&

User Interface (UI)

The User Interface (UI) of the site is what the user sees. Think of it as how the work done in the UX is presented. In our analogy this would be fit and finish of the building working within the plans and guidelines of the UX.

Customer Experience (CX)

The Customer Experience (CX) for a digital product is inclusive of both UX and UI working together. If the UI is good but the UX is bad users can't accomplish their desired task in an intuitive, easy way. If the UX is good but the UI is bad users won't trust the product and get frustrated. Either way users will be more likely to abandon the experience before completing their task.

In other words, you tap or click on weblinks or buttons, the application leads you through a further series of sequenced, process-driven taps or clicks, and voila! You now have a new account and an e-mail notification to alert you of the new account and account activity. In reality, the e-mail system is not a part of the banking account system, so data and/or process orchestration software combine to coordinate the process, exchange data, and create e-mail notifications. Even with all the complicated processes going on "behind the scenes" as financial legacy systems are integrated, you are delivered a seamless customer experience resulting in user-friendly applications now at your disposal.

You may be wondering how these concepts apply to the clinical research enterprise. Similar to the evolution of other industries, the drug/device/biotechnology sector's reliance on research professionals, both internally for preclinical development of potential new products and through

contract research organizations and study sites for testing of the same in humans, grew organically to meet the demand of the global market under constant regulatory scrutiny, as well as inorganically to capture segments of the market it wanted to capitalize. Over time, more functions and departments were created and organized to complete the tasks that required specific knowledge (or what was deemed specific knowledge).

The additive result of organic and inorganic growth is that each newly organized function or department within the sponsors of research, their subcontractors for managing studies, and the sites at which the research is actually conducted seemingly required its own software to solve its own problems without the users fully evaluating what they were trying to solve in cooperation with each other.

Today, we have multiple functions conducting slightly different tasks with much of the same data in hundreds, if not thousands, of different software systems and are living in a very big plate of people, process, systems, and data spaghetti.

This approach has increased technical debt over the years, leaving drug developers, for example, with about the same timeline of 12 to 15 years to bring a new product to market, increased costs to go to market, and an absolute necessity for corporate digital strategy leadership.{2}

How do we get from the proverbial people, process, systems, and data spaghetti mess to something that is strategic, reusable, and future-enabled? Where do we even begin? In practice, we observe life science executives—under pressure to show progress in digitizing their assigned functional areas—screening their activity universe for digital innovation potential and launching a portfolio of (often disconnected) functional initiatives. However, this approach will only continue to make more spaghetti.

A strategic and data-centric approach is needed to implement and master the true power of digital technology. Digital strategy (combined with business and information technology [IT]) is required to fundamentally redefine the purpose of corporate IT/business missions across functional boundaries, along the entire value chain, and offers deep strategic, data, process, and operational insights.

SIDEBAR: **The Terminology**

Before we dive into technology, process management, and the overall IT landscape, it is helpful to understand the quality management system (QMS), process, and IT vernacular we are using. These terms are merely a guide to better understanding why we identify a problem and then apply a fit-for-purpose solution.

***Digital enablement:** Digital enablement is process of establishing business and IT digital strategies to achieve an intelligent, efficient, and effective business model. Digital enablement focuses on delivering an extraordinary customer experience (CX).*

***Disruptive digital technologies:** Innovative software, applications, and/or technology that significantly change the course of daily activity and/or displaces an established tool.*

***Legacy systems/applications:** Legacy systems are established IT applications. They are generally functionally focused, such as a clinical trial management system (CTMS) or electronic data capture (EDC) system. They can be a commercial off-the-shelve system or custom built and require integrations for the movement of data from one system to another. They do not focus on a process, but rather they are built as database structures/architecture with a frontend user interface/user experience (see below).*

***Swivel chair process:** Swivel chair process is the activity of manually entering the same data in several systems within a process or series of processes. The end-user is effectively swiveling in and out of systems to complete a task.*

***User interface (UI):** The user interface is the actual screens, buttons, and fields (we call them wire frames). The number of clicks, the location of the buttons, the information that is collected, the number of screens to collect, the scroll function, etc. are all functions of the UI.*

***User experience (UX):** The user experience is the overall personal, internal experiences one has with an application. The collection of these experiences determines how end-users interact with the application and their unique experiences. UX works in concert with UI.*

***White space process:** White space is the people, process, or systems gap between process steps or process handovers. For example, a CTMS manages information on the investigator running a trial but does not manage the processes that are required for a successful study launch.*

SIDEBAR: **Manual vs. Automation**

Process data are often not "reused," but instead "recreated," requiring end-users to manually access several systems throughout their day to retrieve, manipulate, and manage the data they need to complete their activities.

Manual pain points: *"Extra time" is required to download, review, and connect data through spreadsheets or other applications, send data to colleagues, and/or upload onto SharePoint/collaborative applications.*

Automation application: *Wraps around workarounds and "white spaces" between legacy systems where automation is typically deployed. This is a great place to utilize a disruptive technology alone or in combination with other automation technologies.*

Automation impact: *Activities are identified upstream and "connected" and/or reused as required. In the downstream environment, activities or processes focusing on the overall process and individual activities or silos that currently exist in most companies are addressed through data reuse.*

The Quality Management System

We see the QMS at the epicenter of digital disruption in life sciences. Its unique organizational position allows the QMS to enable and facilitate a truly connected, end-to-end perspective on data, process, risks, and opportunities along a company's value chain.

To tackle the issues already outlined, we will outline a data-strategic, process-focused, user-centric, and technology-enabled use case for QMS. This disruptive approach is designed to enable better connectivity between activities and functions, and to create an environment of future-proofing which is an industry-sustaining approach as well as a reproducible operational model enabling an offensive, constantly improving, and agile workplace.

The ultimate goal is to create an experience that keeps end-users engaged, is easy to use, and motivates compliant behavior—all while avoiding inefficiencies, such as having to access and transfer data between several systems during daily activities. Among the emerging technologies, digital process automation (DPA), the aforementioned robotic process automation (RPA), and blockchain are currently being "lifted and scaled" into drug and device research and development operations (front and back offices) to integrate/connect the data and end-user (see Table 1).

Table 1: Pros, Cons, and Process/Areas of Impact of Disruptive Digital Technologies

Digital Technology	Pros	Cons	Process/Areas of Impact
Robotic Process Automation (RPA): Point application that leverages computer software to capture, interpret, and integrate data with existing application(s) for processing a transaction, data manipulation, and cross functional communication. The technology is similar to a macro.	- Increased accuracy - Increased consistency - Audit trail - Increased productivity - Increased elasticity/ flexibility - Cost effective - Implementation: relatively easy and quick	- Point solution - May take several automated software applications for one process - Does not "fix" process (bad processes remain bad) - Limited to simple tasks - Not enabled for artificial intelligence (AI)	- Logging into safety application to confirm submission - Monitoring a clinical trial budget for changes and updating system with change - Moving investigator address from clinical trial management system (CTMS) to enterprise resource planning (ERP) system
Business/Digital Process Automation (DPA): Managing data and information across processes and legacy IT systems. This type of automation is built on process and activities with multiple business rules to guide end-users through their workflows resulting in the reduction of swivel chair time, additional point solution costs, resource burn, and offshore investment.	- Process-centric view - Holistic view - Cost reduction - Increased accuracy - Increased connectivity - Audit trail - Increased productivity - Increased elasticity/ flexibility - Reliability - Rules-driven	- Implementation: Generally working across several functions and may be lengthy - Multiple integrations - Requires process mapping - Requires understanding of resourcing - Requires understanding of local business/compliance/ regulatory rules	- Integrating with CTMS, EDC, and enterprise financial software to orchestrate the payment process for investigators and clinical trial vendors - Submitting safety reports from regulatory rules (from regulatory information management systems)

Cognitive Intelligence:	- Collates and automates decision making	- Implementation: More difficult than RPA and other forms of automation	- Managing selection of principal investigators
The ability of computer software and the system to perform tasks autonomously that typically require human intelligence. Examples include visual perception, speech recognition, decision making, and language translation/interpretation. This type of technology enables the end-user to "check" and or monitor the aforementioned examples and eliminate the administrative task of manually entering, translating, or scanning multiple materials to determine a cause/correlation.	- Audit trail - Increased productivity - Increased elasticity/ flexibility - Reliability - Holistic view - Increased accuracy - Educated next best action	- Multiple integrations - Requires process mapping - Requires regulatory scrutiny - Requires understanding of local business/compliance/ regulatory rules	- Digital management of the entire safety process, including initial causality, triage, and signal detection - Managing quality assurance risk and audits
Blockchain: Distributed ledger of information/data that stores a history of all transactions that have occurred within the ledger in a linear/chronological order. Blockchain enables safe and secure transfer of private information within the ledger.	- Increased data quality and accuracy - Increased data access - Increased revenue - Increased data security - Decreased cost	- Newer technology - Still under limited application in research and development	- Investigator qualifications - Operational and back office financial process (over the counter, inventory management, etc.)

The overall IT and business strategies connect business processes, leverage robust master datasets, improve efficiency, and increase transparency/regulatory compliance. By implementing proven technologies and software, companies can leverage existing lessons learned from other industries to increase production, regulate compliance, develop novel programs faster, increase employee satisfaction, and improve customer feedback.

Despite its recent interest in disruptive digital technologies, the life science industry was slow to adopt newer digital process automation tools to develop a holistic, risk-based approach to managing data/operations. Further, the industry mainly focuses on external regulators as the key

customers causing the life science digital toolbox to remain innovatively stagnant and relatively immature compared to other industries. This immaturity is creating significant opportunities for improvement in operations, resource allocation, and systems integration. Examples are:

- Process white space around clusters of documented regulated activities
- Multiple software point solutions
- Multiple workarounds
- Underdeveloped risk management frameworks
- Lack of process/system integration

Disruptive Technologies

Data are the Currency of the Digital QMS

By connecting process data through the use of several synergistic digital technologies, we are now able to manage the process and data across the value chain.

We determined that the following functions and processes would benefit most from digital enablement:

- Preclinical
- Quality
    - Audit management
    - Risk management
- Clinical operation/Early development
    - Study start-up
    - Contracts/Third-party vendor management
    - Clinical supplies management
- Pharmacovigilance/Drug safety
    - Contracts/Third-party vendor management
- Regulatory affairs
    - Regulatory application process
    - Contracts/Third-party vendor management
- Medical affairs
    - Contracts/Third-party vendor management
    - Call center management

The Cost Impact

Multiple forms of automation can be used to assess the people, process, and IT landscape and enable the right technology at the right place at the right time. Further support of automation as the digital currency of the future comes from The Institute for Robotic Process Automation, which has seen a cost reduction of 35% to 45% for onshore operations and 10% to 30% for offshore operations. Gartner has claimed that 30% to 40% of existing business process services are likely to be impacted by automation.{3}

The Benefit/Risk Balance

Today's automation technologies reduce white space processes between legacy systems by securely connecting and or interfacing with historically hard to interface legacy systems. Generally, automation mimics human action and eliminates the need for the end-user to connect multiple systems to complete one's activities or tasks and/or focus on value-added, critical activities.

By utilizing and combining the aforementioned technologies, automating the business processes enables the employee to move through and work around the white spaces while the system pushes the next activity to the employee. Instead of manually beginning the next activity, the employee is automatically prompted. This process automation can achieve the following for any business:

- Reduce direct and indirect costs
- Improve accuracy, consistency, and reliability
- Process complex, high-volume activities more efficiently
- Improve process controls and risk-based approaches
- Increase agility and improve operational management offensive
- Integrate workflows for a more seamless approach
- Connect data sources
- Reduce cost of quality
- Offer more transparency for better decision making

Not all technology is created equal and there are inherent risks in selecting and implementing automation technology. What are the key risks and potential issues for enabling a fully automated QMS?

- **Complexity:** Due to the rapid growth and evolution in technology, it may be difficult to assess if the right technology has been selected or if there is a better less expensive technology in the pipeline.
- **Scalability:** Another question to consider is whether the tool or technology is scalable and fit for purpose. In some cases, the technology is fit for purpose and does not need to scale up or down to connect to other upstream or downstream processes. However, in some cases, the technology/tool will need to scale up to adjust for global requirements. Proper assessment of the tool would define the risks of fit for purpose and scalability.
- **Change:** Finally, how will the technology keep up with the change in regulatory agency modernization and the potential change in standards? Simply put, today's automation needs to be prepared to meet tomorrow's regulatory expectations. Again, this analysis is accomplished by conducting a proper assessment of the technology and its history to perform, update, and integrate over time.

How does the industry continue to facilitate change and influence automation technology? First, finding and adapting mature software that is being used successfully in other industries is key.

Imagine sharing data to enable better patient safety data or clinical outcomes, or sharing concepts and lessons learned in working groups or open research forums. It's all possible with the right technology that ensures data are entered once and reused, not recreated.

The ultimate success when introducing a new drug/device/biotechnology product is defined by production results in the least amount of time and cost possible. All the while, the product must be safe, efficacious, and compliant with regulatory demands. These standards lead to multiple functions and tasks within a manufacturing process that must be managed in increasing tedious detail.

No matter how a new pharmaceutical product is produced, the end result must deliver an experience that keeps end-users engaged, is easy to use, motivates compliant behavior, and avoids inefficiencies, such as having to access and transfer data between several systems during

daily activities. Among the emerging technologies, DPA, RPA, and blockchain are currently being "lifted and scaled" into clinical research enterprise operations (front and back offices) to integrate/connect the data and end-user together. The overall IT and business strategies are to enable connected business processes, leverage robust master datasets, improve efficiency, and increase transparency/regulatory compliance.

Conclusion

Digital strategy provides capabilities to move information through process automation. Leveraging existing data systems and tying them into an automated process reduces manual document creation.

The goal of digital strategy transformation drives a rethinking of an organization's service model delivery. Coupled with streamlining processes across existing silos and improving efficiency, directed actions or decisions drive business functionality. Improved digital interaction capabilities enable increased production and drive experience. As a result, customer satisfaction is improved through transparency.

Aligning with a QMS, a disruptive approach designed to enable connectivity, sustainability, and continuous evolution fosters agility in the workplace. Fixing the foundation to implement a digital strategy fundamentally redefines the business mission, improves customer experiences, and improves the bottom line.

References

1. https://www.linkedin.com/pulse/robotic-process-automation-revolution-business-technology-patel/?articleId=6675755793763049472
2. https://www.protiviti.com/sites/default/files/united_states/insights/board-perspectives-risk-oversight-technical-debt-limiting-competitiveness-issue109_protiviti.pdf
3. https://www.gartner.com/en/newsroom/press-releases/2019-10-02-gartner-says-robotic-process-automation-can-save-fina

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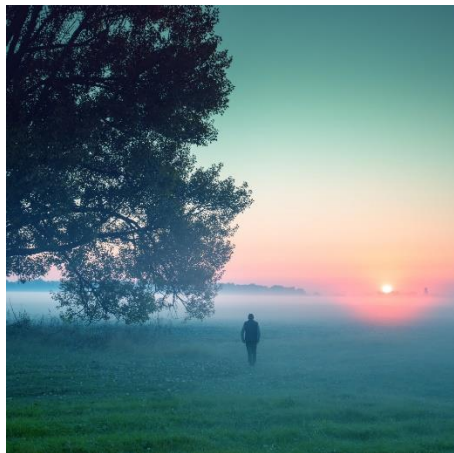

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OPINION

You Believe in Diversity, Equity, and Inclusion? Get Out.

Allison Kalloo, MPH

Newsflash: Minorities—African Americans in particular—over-index in measures of poor health outcomes. By now, you already know that combating a deadly plague has only been exacerbated by persistent disparities in disease prevalence and by the stark and longstanding underrepresentation of communities of color in clinical trials. The fierce urgency to identify effective coronavirus solutions means these inequities may finally be getting the exposure long needed.

Amid our collective despair, tiny celebrations are taking place in honor of silver linings and tipping points. This surreal period in human history confirms for me that there is no better time to dream than in the darkness.

COVID-19's toll affects us all, but the stark disparities evident through the lens of race reveal that the heaviest losses are among Black, LatinX, and Indigenous Americans—more than twice as high as the rate for Whites and Asians. Massive attention is now focused on getting Black and Brown people to participate in clinical trials in numbers that reflect disproportional disease burden. The world has also been given a primer on the effects of unresolved baggage regarding race and racism and how sociocultural variables reverberate in clinical research.

If we didn't know any better, one could assume from the global coverage regarding COVID-related disparities that civilization has uncovered a new problem. In reality, the void in diversity,

equity, and inclusion (DEI) in research is an old problem. What is unprecedented is the widespread attention.

In truth, the current focus on lack of DEI in clinical trials has brought moments of delirious intoxication. Could it be that industry has awakened to the obligation and opportunity of change for the better? Has industry now developed an appetite for implementation that will be followed by decisive action? You may say I'm a dreamer.

Eternal Vigilance is the Price of DEI

Kindly overlook the fact that I must temper my glee. If my hopefulness is tinged with incredulity, I have my reasons. For all of the potential good that is to come, I am hypervigilant about not allowing this bright spotlight to blind me to the unhealthy patterns of the past. Broken promises and disappointments have left serious adverse events in the form of little burn spots. DEI projects with promise have been whitewashed or underfunded or put off for another time. Industry commitment has in fact been lost to follow-up.

Please understand that the fierce urgency of addressing the racism of a virus also means opening up a secondary vulnerability to grandiose promises. What communities of color are really susceptible to is facing another screenfail by fully engaging our hopes and dreams again to no avail. To truly believe that this moment has gravitas and real staying power, those of us at highest risk for cynicism will need concrete evidence of industry's commitment to resolving disparities.

I am personally expecting an evolved set of metrics. This time, I am going to need to see the receipts for all of the words. But I'm not the only one.

No doubt, the history of medical apartheid factors largely into African Americans' hesitance to participate in the very research likely to save lives. Look no further than the data on coronavirus infections and deaths showing an ironic and tragic inverse of the numbers of vaccinations by demographic. One might conclude that marginalized populations are unaware that the Tuskegee Experiment was singularly responsible for the advent of informed consent and heightened patient protections by federal regulation. You ask why we have not come running.

The industry needs help communicating about what vested interest in research really means, and the pandemic is poised to drive the point home. There has to be a reconciliation of these facts with all stakeholders—that when studies do not reflect the diversity of the real world, not only will modern medicine continue to be complicit in perpetuating disparities, but those minorities who categorically refrain from participating in research will be complicit in less than favorable health outcomes and our own demise.

This is no time to sugarcoat the facts. I tell people as often as possible that we simply cannot afford to sit this out. Frankly, we should consider inclusion in clinical research as much a social justice issue as protesting against police brutality.

Practice What You Preach

Make no mistake. My role as disruptor includes being a staunch advocate for patient diversity in clinical trials and actually stepping up to participate. I have been in more than a dozen studies and I am currently participating in the Novavax vaccine trial. But advocating that patients of color take risks—when industry is so risk-averse and has been heretofore unreliable—creates its own anxiety.

These communication challenges inherent to issues of diversity, inclusion, equity, social determinants, historical injustices, and so forth—whether real or imagined—bring about additional obstacles downstream when trust must be negotiated. But here is where we must start: Whether it's a matter of hiring Black staff, recruiting Black executives, asking Black community members to join your community advisory boards, contracting with Black-owned companies, or asking a member of your patient advocacy group to lend some perspective to publications calling for more diversity in clinical trials, I can guarantee that we all do some form of the following calculus in our heads.

Are you really ready for the truth? Can you handle it? And if you can, will there be tangible evidence of the changes we recommended? And what will be the price for making the establishment uncomfortable or disrupting the status quo?

We—Black and Brown people—are not inspired to believe you when you say that diversity is important to you if you don't put skin in the game. Making public statements that include the phrase "Black Lives Matter" will fall flat without adequate follow through. What will your ethos matter if you don't actually DO something? It is no longer acceptable to *say* that this is not acceptable. We have no use for your anger. We need your action.

Epic, concrete, and systemic changes are needed and will be the only context under which real clinical trial diversity will transpire. Wherever the shoe fits, consider the cognitive dissonance you bring about when you allow these scenarios (and in no particular order):

- Do not treat Black and Brown communities as monolithic groups that have the same life experiences, backgrounds, income, education, language, customs, interests, attitudes, and opinions in common. We don't.
- Do not pile people of color into presumptive stereotypes and shallow narratives, not the least of which is that Black people can only be reached through the church. Not true.
- Do not presume that distrust among Black people is tied only to Tuskegee, Henrietta Lacks, eugenics, and other infamous atrocities of the past. Today's racism is more relevant to reluctance.
- Factor in relevant disease prevalence data—or acknowledge patterns of participation disparities in those areas—when designing protocols or planning recruitment initiatives.
- Beware feelings of privilege that allow the National Institutes of Health (NIH) mandate for inclusion to be ignored and enrollment to be closed without adequate minority representation; AND, check yourself when NIH allows continued federal funding despite noncompliance.
- Do more than "just enough" to comply with the U.S. Food and Drug Administration's expectations of your New Drug Approval application, and spend more time investing in a real plan to prevent shortfalls than in crafting the explanation for them.
- Refuse to allow mere familiarity or convenience to be your site selection criteria, especially when those sites have no demonstrable reach in that community beyond their location.
- Never presume a team approach or a collaborative mentality and rely less on physician referrals to fill your study's patient rosters.

- Provide physicians with easily accessible education about clinical trials allowing them to embrace medical research as a viable treatment option.

- Do not allow study goals and timeline to blind you to real people being the end-user; humanizing your workflow leaves room for humanizing the patient experience and establishing a foundation for trust.

- Put your studies through mock trials for a reality check through the lens of the patients you wish to enroll; when seeking to broaden DEI, check the protocol for inclusion/exclusion criteria that double as barriers to diversity, equity, and inclusion at your study's gate.

- Put gatekeepers through sensitivity training developed by people of color.

- Bolster and guard your patient recruitment budget and make sure it is not allowed to become an afterthought.

- Make space, set aside resources, and allow time for an external task force to review and assess cultural sensitivity and patient centricity of study protocols so as to identify biases and barriers.

- Stop defaulting to doing business with majority-owned (read: White) marketing firms to resolve minority representation simply because they seem "safe" and familiar.

- Stop allowing fear of change to force a default to using status quo recruitment and retention activities simply because they seem "safe" and familiar.

- Establish quantifiable recruitment expectations for recruitment brokers based on demographics that reflect known data about the therapeutic area.

- Refuse to second-guess the pricing, professionalism, scalability, and ability to deliver the goods and services because it is a small, minority-owned business, especially when you would be less likely to treat a larger business of privilege with comparable scrutiny.

- Never solicit feedback from consultants (whether professionals, study participants, patients, or members of the community) and then fail to implement their recommendations; likewise, ensure credit and compensation where due.

- Stop cloaking your perception of expertise in whiteness first.

- Stop expecting study participants to take risks while you remain risk-averse in every possible way.

- Do not double down on disparities by setting conference fees that make attendance prohibitive for vendors of color (often classified as historically underutilized businesses [HUB] and/or certified minority- and women-owned businesses).

- Compensate keynote speakers to address diversity, equity, and inclusion, and make a sincere effort to book Black or Brown experts; also, don't expect these experts to provide that expertise *pro bono* in this environment.
- Make certain your website's homepage contains a "DIVERSITY, EQUITY, AND INCLUSION" section to demonstrate that you're practicing what you preach about the DEI priorities of your organization.
- Allow transparent updates and real metrics around your dedication to diversity, equity, and inclusion, and be willing to be held publicly accountable.

Broken, But Not Beyond Repair

While the system has long been broken—and addressing it will require more than statements—I recognize the value in framing these issues in such a way that you will *know* that solutions are within reach and that there is a tantalizing variety (read: diverse array) of people, organizations, policies, and clinical interventions poised to change the landscape for the better.

In the meantime, know that It will take much more than throwing a fistful of money at a rescue attempt rather than planning better from the beginning.

Take a hard look at the participant invitation list created by your protocol design. The code for diversity, equity, and inclusion is written there in your inclusion/exclusion criteria.

If you are sincere about filling the studies of tomorrow with a broader spectrum of individuals, implementing the tools of transformation will require the guts to be honest with yourself about your commitment to see it through.

Don't expect that attitudes about participating in research are distinct from how a person feels the system treats them or looks out for them. African American professionals and high-income earners—even those who work within industry—often express concerns about participating in research. Others of us who actively promote DEI in clinical trials deal with misgivings that linger.

Reconciling these issues is fundamentally a matter of perception. Getting to a better place in DEI efforts will demand significant outreach going forward—both broad and deep. Lamenting lack of diversity in studies while not going out of your way to do the work of making it better is business as usual. Engaging with underrepresented communities of color may require a departure from the status quo, but it's not rocket science when you're intentional.

Dedication to diversity, equity, and inclusion? It's cliche without decisive action. To validate, consider this top 10 list:

1. Humanize the process.
2. Invest in relationships that serve all parties.
3. Connect when a study is not hanging in the balance.
4. Build infrastructure that will pay dividends.
5. Invest in community-based relationships.
6. Partner with skilled interpreters.
7. Listen to patients.
8. Implement.
9. Keep your promises.
10. Repeat.

Reaching communities of color pivots on those in charge of clinical trials *being more trustworthy*. In other words, you first. Show us what you're working with.

As for me, nobody is more interested to see how this goes.

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GOOD MANAGEMENT PRACTICE

Diversity in Clinical Trials: Going Beyond *Why* to *How*

Scott Gray

It's no secret that patient diversity is a major issue in clinical trials, and that a lack of diversity makes it difficult to measure efficacy and safety. However, even given the U.S. Food and Drug Administration's recent guidance, there is not a lot of actionable advice for trial sponsors and research organizations looking to increase enrollment among historically underrepresented groups. The conversation has stalled at *why,* and the time is long overdue to start talking about *how*.

The Benefits of Diversity in Clinical Trials

One goal of all clinical trials should be to represent the affected population as a whole. Because most conditions are not specific to a single demographic, sample populations shouldn't be either. Ethically, a lack of representation in trials raises concerns about ensuring equal access to new treatments and cures. A person's socioeconomic status or demographics should not exclude them from participating in a clinical trial or from being assured the approved treatment will be safe and effective for them once approved.

Historically, 60% to 70% of clinical trial participants have been white males because they were the ones who could afford the cost of travel and the time off work to participate. Today, ethnic diversity in clinical trials continues to be an issue. For instance, in the United States, African Americans make up 13.4% of the population, but only [5% of clinical trial participants](). The disparity is even worse for the Hispanic or Latino population; they make up 18.1% of the U.S. population and only 1% of trial participants. Asian Americans account for 6% of the population and only 1% in clinical trials, and two-thirds of clinical trials are absent any Native American participation.

Such lack of diversity is not limited to U.S. trials, however. One recent study of trials across 29 countries over the past 21 years shows that [86% of participants were white](). The disparity is concerning because it is scientifically crucial to understand how a new drug or therapy affects patients of varying ages, genders, and ethnic backgrounds, as reactions to many new treatments are proven to differ depending on the individual's demographics. For example, African Americans react differently than white populations to certain blood thinners and [asthma medications]().

Proportional representation in clinical trials helps to accurately understand how or if a drug affects a particular demographic group negatively or differently. More investigation can then define the issue or address it before the therapy receives approval. Representation is essential because once a drug is commercially available, access will not be restricted to certain demographics, so a clear understanding of each demographic's reaction is an imperative *before* going to market.

Practical Methods for Overcoming Barriers to Participation

To achieve our shared diversity goals, we need to directly address the challenges historically underrepresented populations experience in clinical trial participation. Many of these barriers could be mitigated through improved communication with targeted populations. Educating each group on the importance of trial participation and the potential benefits for participants can go a long way to increase enrollment. For instance, ensuring these groups are aware of the compensation and travel stipends available can sway patients to become participants. In the U.S.,

this might include discussing the Ensuring Access Act, which deducts the first $2,000 a patient receives for clinical trial participation from federal benefit eligibility determinations and aims to remove some of the financial barriers lower-income families experience.

This type of education requires dedicated resources for community outreach, including building relationships with community leaders in underrepresented demographics to act as knowledge ambassadors. It should also include direct communication with patient advocacy groups, patients and caregivers, and physicians to help inform the design of clinical trial protocols to mitigate any steps that discourage participation.

Additionally, trials can be designed with more resources and communications to make trial participation less burdensome for participants. For example, choosing payment or reimbursement methods that best serve a particular population and partnering with companies that manage patient logistics and expense prepayment can significantly reduce the barriers to participation and improve retention rates in trials.

By providing direct support to patients from enrollment through the end of the clinical trial, these services ease the financial, logistical, and psychological barriers to participation. Where possible, increasing site locations in communities with high populations of underrepresented populations and holding recruitment events during weekend and evening hours can also make trials more accessible.

Addressing these challenges may not only increase participation, but also increase the participants' satisfaction with the entire experience.

How Dedicated Patient Coordinators Impact Trust and Retention

Recruiting diverse populations to participate in trials is only the first challenge. Participants must be supported and remain in the trials through completion in order to be represented in the trial outcomes. Partnering with a company that provides patient logistics coordination and patient support may be one of the best tactics available to improve retention rates while reducing the burden on trial staff. By providing coordinators who are assigned to each participant through the length of the trial, patients receive personalized support for travel, financial prepayments or

reimbursements, pandemic-related issues, relocation services, and other logistical support they may need.

These services are most effective when coordinators provide one-on-one support and are matched with participants based on things like location or time zone, culture, and language. This approach reduces the burden on participants and caregivers, allowing them to focus on their health and improves trust and satisfaction with the experience, increasing the likelihood that a participant will remain in the trial through completion.

Unique Challenges in Global Studies and Studies of Rare Diseases

Achieving diversity in clinical studies involving rare and ultra-rare diseases presents its own challenges. There are significantly smaller patient populations available in rare disease studies, so special efforts are necessary to recruit and retain them. In the rare disease space, a specific clinical trial may be the patient's only hope for medical treatment, so including them isn't just ethically necessary; it's also medically necessary.

In these cases, extensive travel is generally unavoidable as patients may be spread out across the world, or in the case of a genetic condition, multiple patients may be concentrated in one specific geographical area in a different country from the clinical site. For example, a significant amount of research may be done at a single site in Frankfurt, Germany, but the babies who would benefit from this life-saving research are clustered in China and India. In these cases, entire families may need to relocate to Germany for months, requiring airline travel where medical equipment is permitted on-board the plane, apartment rentals, translation services so the family can communicate with medical staff, and more.

Additionally, patients may be very ill or have diseases that are debilitating and impact cognition or mobility. A patient's location or ability level should have no bearing on his or her right to participate in a clinical trial, but these factors do present challenges.

This is another area where patient logistics companies can provide invaluable support to improve trial performance. Their trained coordinators understand the medical challenges faced by patients and caregivers and can provide complex cross-border support, translation and interpretation

services, and logistics management for participants in remote locations or with complex medical needs. Their needs might include visa and passport procurement, managing exchange rates and reimbursement, navigating local regulations, and coordinating multi-leg travel and relocation efforts.

When you consider the complicated nature of participating in rare and ultra-rare disease trials, it is no wonder that drop-out rates are typically relatively high for these types of studies. It has been shown that 85% of all clinical trials are delayed due to not retaining enough participants to continue, and that the cost of just one patient dropping out of a rare disease trial far exceeds the average cost of losing a participant in a common clinical trial of approximately $20,000. Considering how expensive and time-consuming it is to lose a patient, investing in services that increase retention rates and retain diverse participant pools once they are recruited is a logical choice.

Diversity is Our Responsibility

We can all agree that achieving diversity in clinical trials is complicated. However, with these specific steps to improve community outreach, education, and accessibility—along with an investment in retaining those populations once they are recruited—adequate representation is achievable.

Scott Gray is co-founder and CEO of Clincierge, a firm focused on patient logistics management for clinical trials.

THE LEGAL LANDSCAPE

Show Me the Money: Strategies to Increase Trial Revenue

Robert King

Medical researchers are not supposed to be motivated by the prospect of profit, but we all have bills to pay. With billions of dollars riding on research, regulatory agencies guard against kickbacks camouflaged as legitimate compensation. To prevent abuse, site payments must not exceed "fair market value" (FMV).

However, no word in the English language is more open to interpretation than "fair."

So how can a site get paid more, while staying in step with regulations?

The Lay of the Land

Typically, sponsors provide all sites with the same initial budget, but geography, the site's business structure, and the site-specific target recruitment population can all impact costs. For example, Mississippi has the highest obesity levels in the United States, while Colorado has the lowest; this could raise recruitment costs for a diabetes study at a site in Boulder, as compared to a different site in Biloxi.

As a result, compensation that is completely acceptable for one site would present regulatory risks elsewhere. Sites that can present information that demonstrates justification for higher compensation will be better positioned in budget negotiations.

Building that case begins with understanding how sponsors and auditors conduct FMV reviews. Generally, their focus is not on the amount of the payment—though a "high" payment can result in heightened scrutiny—rather, they determine whether the process for reviewing budget demands was reasonable and whether, given the site's specific characteristics, the payment amount was "fair" as determined by the process. Let's look further into these concepts.

It's a Beautiful Day in the Neighborhood (*Fred Rogers*)

Immediately upon receiving a protocol, each potential medical procedure should be identified. Any duty that is not compensated should be reviewed to determine whether it is appropriate to seek compensation.

The sponsor's offer for each procedure can then be measured against subscription databases that document medical pricing. Be sure to look at geography when conducting this analysis. Regional pricing differences can be considerable. Also, do not be fooled into thinking that this only applies to high-priced locales like New York City. Data indicate that states you would not first suspect, such as Kansas and Nevada, often have above average pricing. Sites located in higher cost regions have a tremendous advantage in gaining budget concessions, even if a site's own costs do not reflect higher regional averages.

Art is Making Something Out of Nothing, and Then Selling it (*Frank Zappa*)

Most universities place surcharges to recover indirect and overhead expenses on costs associated with research. A random search found surcharges at Duke, Penn State, and Tufts could rise above 60%. Meanwhile, San Jose State was a "bargain" at 46.5%.

These surcharges often apply not only to procedures mandated by the protocol, *but also to pass-through expenses* such as compensation paid to study subjects or travel costs. The surcharge in effect converts reimbursements into a new revenue stream.

In setting an appropriate surcharge, the site must weigh the risk of discouraging sponsors approaching them with offers of trial participation against the potential increase in profitability when they are selected. Once the site settles on an appropriate surcharge, it should create a formal policy to that effect. This policy should be approved by the highest echelon of the site's leadership, and the site should then be prepared to quickly provide a copy of the policy to sponsors upon request.

Once the policy is in place, sites should treat the overhead rate as non-negotiable, since failing to treat the overhead rate as set in stone is out of step with most institutions and could be viewed as a red flag.

All Advocacy is, at its Core, an Exercise in Empathy (*Samantha Power*)

If you work at a study site, who are you to the sponsor? Before you answer, peel back the layers of the question. Who are you in the context of the study under negotiation? Is the principal investigator a thought leader in the field? Does the site have a good long-running relationship with the sponsor, or has your relationship been troubled? Specifically, has the sponsor been happy with your past recruitment efforts and the timeliness of data submissions?

The answers to these questions all contribute to how motivated a sponsor may be to initiate a site. By developing relationships with your opposites, you can obtain answers to these questions that will inform your strategies for budget negotiations.

To Know Your Enemy, You Must Become Your Enemy (*Sun Tzu*)

In budget negotiations, site leaders must think about FMV as a sponsor would.

Sponsors often view the issue of specific procedure pricing and the amount of the overhead charge as two separate and unrelated issues.

Is the overhead charge reasonable? Check.

Once a sponsor agrees to pay a demanded surcharge, they tend to not to think about it. As a result, the impact of overhead surcharges just might be ignored when a sponsor conducts an FMV analysis, and this may open the door to greater site compensation.

Here's how it might play out. A sponsor offers $14 for a procedure. The site needs $17 to break even, which it requests. Following FMV review, the sponsor makes a "drop dead" offer of $15. The site now has four bad choices:

- take a loss on the procedure;
- walk away from the study;
- keep pushing for a higher price, which is unlikely to be successful; or
- attempt to get a higher price on other procedures to "subsidize" the loss.

However, if the sponsor had previously accepted a site overhead surcharge of 20%, then the sponsor's $15 offer translates into a very satisfactory $18 fee.

The boost provided by the overhead surcharge will reduce the number of items that are in contention and make those that remain easier to resolve.

That Which Costs Little is Less Valued (*Miguel Cervantes*)

Sites must guard against losses when recruitment falls short. One way to mitigate this risk is to identify each department that is involved in the protocol and to review the Clinical Trial Agreement for uncompensated site duties. This identifies fees where the sponsor might be open to additional or upfront payments.

Since start-up fees will be paid regardless of whether recruiting goals are met, they are ideal for preventing losses when recruitment is subpar.

Some examples are:

- Pre-award services
- Pharmacy and radiology start-up fees
- Institutional review board fees

Charges for services rendered after the study's completion may also be available, such as follow up phone calls and close out costs like the costs associated with audits and document storage fees.

We Know the Future Only by the Past We Project Into it (*John Lewis Gaddis*)

When there is a realistic chance that a site will participate in more studies with a particular sponsor, it would be helpful to develop a master site budget for such engagement. By reaching agreement on recurring costs and fees, negotiation times can be slashed. To ensure that the fees remain current, the agreement should include a clause that permits the site to periodically increase fees without mutual agreement, subject to reasonable limitations (e.g., annual price increases up to the rate of medical inflation upon notice to sponsor).

If a master site budget is not feasible, but the site has worked with the sponsor in the recent past, then before budget negotiations begin a review of the previously paid fees and costs should occur. Many such items are not protocol specific; using them as support for the agreement currently under discussion permits the site to avoid re-negotiating fees.

Conducting such a review prior to new budget negotiations also allows the site to identify those areas where its historic fees are no longer sufficient. Sites should anticipate that sponsors will have concerns in such circumstances and should be prepared to demonstrate why specific higher fees are now required. Otherwise, resistance may be expected.

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Professional Patients in Clinical Trials—A Serious Issue That Hampers Research

Salman Rashid

COVID-19 is a force that has affected virtually everyone in one way or another. Most of us have gotten used to wearing masks outside our homes, using sanitizers regularly, practicing social distancing, avoiding large gatherings, and washing our hands regularly. The novel virus has also pushed a lot of topics to the forefront, such as telehealth, remote work, and clinical trials.

Clinical trials used to be a niche topic that was discussed primarily among healthcare professionals and stakeholders working for contract research organizations (CROs), study sites, patient advocacy organizations, and pharmaceutical companies. However, the pandemic made it a household topic. "Which pharmaceutical company will come up with THE vaccine?" "Which trial is in which phase?" "How long will it take for a trial to provide a safe vaccine?" Everyone was asking these questions.

While only a handful of vaccines received emergency use authorization (EUA) after thorough testing (with Johnson & Johnson's being the latest one), there are numerous vaccines that didn't see the light of day. When it comes to clinical trial failures, most researchers would list the lack of efficacy, data inconsistencies, safety issues, lack of funding, or protocol errors as primary reasons; however, there is another factor that often flies under the radar but causes major issues—the challenge of dealing with "professional patients" in clinical trials.

What are professional patients and how do they hamper the integrity and efficacy of clinical trials? To understand that, let's take a look at how clinical trials have been impacting our lives and preventing diseases in the process.

Clinical Trials in a Nutshell

Clinical trials are nothing new; many pharmaceutical companies (with help from CROs and study sites) and independent investigators have been conducting drug and medical device studies with human subjects for decades. The typical goals of such trials are quite simple—improving health, curing deadly diseases, or reducing recovery times. In fact, many clinical trials result in therapeutic breakthroughs that can effectively treat what were previously untreatable conditions.

However, clinical trials are far more difficult and complex than they usually appear to outsiders. Such studies can cost billions of dollars, take an average of around 34 months to complete for a product that makes it to market, require numerous regulatory approvals across multiple phases, and include patients that need to voluntarily enroll in and comply with what are often complicated protocols—something that can heavily influence the reliability of the data and the efficacy of trials.

Patient recruitment poses a significant challenge for any given clinical trial. Finding patients with the specific conditions required, diversifying the sample, providing them with ample motivation, and ensuring retention until the end of the study are challenges themselves. Vetting patients effectively before enrolling them is another crucial component. However, despite best efforts to weed out potentially bad apples, many professional patients still make it through the process and have the potential to cause billions in losses.

What are Professional Patients?

Also known as "duplicate subjects," professional patients are individuals who frequently participate in clinical trials for nefarious reasons. Some even participate in multiple studies simultaneously—yes, it happens all too often! Let's take a closer look at the most common types of professional patients.

The first type of professional patient participates in clinical trials just for the financial compensation. While these patients do check the box of being "healthy" or having the required medical conditions (depending on the inclusion/exclusion criteria of different phases and types of studies), getting paid to participate leads them to sign up for multiple studies—either subsequently or simultaneously. These patients may receive several doses of drugs from different trials in very short timespans that not only affect their health, but can severely impact the trial or study data through drug-drug interactions. While one or more of the drugs may have been promising, overall results can be skewed by patients who fail to display the expected benefits due to drug effects from other trials in which they are secretly involved. This can lead to costly repeats of trials.

The second type of professional patient is far more dangerous. While they do have the required health conditions, they are in it for the drugs. This can be commonly seen in research regarding addiction treatment and drug abuse. How exactly do these professional patients hamper research data? Well, they fake the results during trials in hopes of upping the dosage and gaining access to more drugs. Once again, this can lead to data quality issues, causing effective drugs to be announced as failures.

The third type of professional patient is one who falsifies his/her information right from the start, purely for financial gain. They don't have the required condition(s), but use different strategies to participate in trials—and some of them even get enrolled! In these cases, testing data are manipulated from day one and, during the trials, the data quality will worsen even more as these patients never had the required conditions to begin with.

The Fallout from Professional Patients

As outlined here, the participation of professional patients in clinical trials leads to inaccurate data collection and hampers the integrity of studies. Sponsors, CROs, pharmaceutical companies, and other stakeholders spend considerable time and resources to set up trials, recruit patients, and go through the various phases.

Even if the drug or treatment is promising, professional patients can make the data inconsistent enough to shut down the studies in which they are involved. Not only does this cause millions of dollars in losses, it prevents promising drugs from progressing beyond the preliminary phase(s). Who knows, maybe some professional patients were involved in clinical trials that were focused on a COVID-19 vaccine!

Preventing Professional Patients in Clinical Trials is Crucial

While participating patients are vetted through the informed consent process and an impartial institutional review board, it might not be enough to prevent professional patients from slipping through the cracks. They are constantly finding ways to falsify information so they can participate in trials.

More thorough vetting might be required alongside an effective patient identification system. Coupled together, this could help red-flag known professional patients, prevent massive losses, and significantly improve the efficacy of trials.

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SITES & SPONSORS

The Modernization of Clinical Trials: COVID-19's Lasting Impact

Mark Clements, MD, PhD, CPI, FAAP; Komathi Stem, MS

COVID-19's effect on clinical trials is a tale of two outcomes.

Near-term, the pandemic has been devastatingly disruptive. About 80% of non-COVID-19 trials were either stopped or interrupted.{1} As of January 2021, COVID-19 had stopped more than 2,000 clinical trials.{2}

But, like a wildfire that cracks open the cones of sequoia trees to release their seeds, COVID-19 has germinated widespread adoption of underutilized trial models, tactics, and tools such as virtual/decentralized clinical trials (DCTs), telehealth visits, remote patient monitoring (RPM), and the use of real-world data (RWD). These new practices have taken root and will have a lasting impact on how clinical trials are designed and conducted.

DCTs: The Cat's Out of the Bag

In 2015, the Clinical Trial Transformation Initiative (CTTI) recommended that trial sponsors consider fully or partially decentralized DCTs, defined as trials executed through telemedicine and mobile/local healthcare providers.{3} Although a shift toward virtual trials has been gradually building, many sponsors have been hesitant to adopt this model due to concerns about whether their trials would be accepted by the U.S. Food and Drug Administration (FDA).

Thanks to COVID-19, these worries have dissipated. With a nationwide lockdown issued in March 2020, the FDA recognized the safety risks of in-person clinical trials and issued guidance

encouraging researchers to consider alternatives for patient assessments and data collection, including virtual visits, remote data collection, and RPM.{4}

Almost immediately, the popularity of DCTs skyrocketed. Before the March lockdown, one company that supports virtual clinical trials had about a dozen calls a week from potential clients. By June, it was receiving hundreds of weekly inquiries.{5}

For years, patient advocates have been pushing for more virtual trials to make participation easier. At the same time, trial sponsors, contract research organizations, and study site investigators have recognized that DCTs can:

- Remove obstacles to patient enrollment and participation, the top cause of trial delays or terminations.
- Reduce high rates of participant drop-outs, which rose from 15% in 2012 to 19% in late-stage studies globally.{6}
- Increase diversity in patient populations.
- Provide participants with greater control, convenience, and comfort.

Although elements of the DCT model (full or hybrid) can be integrated into any clinical trial, this approach is especially suitable for studies that collect physiological data from devices in the patients' home (e.g., blood pressure cuffs, glucose, and insulin dosing data).

Having proven their mettle in the cauldron of COVID-19, DCTs are here to stay. As Esther Krofah, executive director of the Washington, D.C. think tank FasterCures, notes, "We're going to see virtual trials as a new, normal part of clinical research. The cat is out of the bag."{5}

Digitization Improves Patient Access and Participation

The FDA's embrace of DCTs has accelerated the digitization of all aspects of clinical trials, from design and patient recruitment to data collection and analysis. For example, by taking advantage of robust patient databases and sophisticated social media tools, sponsors can not only increase awareness for their recruitment campaigns but also more precisely target the right patient populations. Researchers from Harvard and MIT report that digitized DCTs may help increase

trial access and diversity, especially for women and participants from rural areas and racial groups traditionally underrepresented in clinical research.{7}

Perhaps most importantly, telehealth visits and the use of remote monitoring tools can remove barriers that prohibit patients' full participation for the duration of in-person trials. By minimizing or eliminating problems with transportation and infrequent communications, clinical trials can become part of participants' everyday lives. This will allow investigators to more easily, effectively, and precisely track how each patient is responding to treatments and intervene as needed in real-time. In addition, the trial data will provide more meaningful insights about patients' real-world experiences with the drug or medical device under investigation.

RWD Comes of Age

For more than a decade, clinical trials have been collecting and using RWD, whether self-reported by the patient or from mobile devices, wearables, or other biosensors. In the past year, however, as COVID-19 made remote trials the new normal, RWD have become an integral element of trial protocols.

This trend began to gain momentum following the 2016 passage of the 21st Century Cures Act and the FDA's launch of a program focused on using RWD and real-world evidence (RWE) to support regulatory decision making, including approval of new indications for approved drugs and biologics. The FDA also encouraged researchers to consider situations where RWE trials could generate useful information.{8} Today, medical product developers are using RWD and RWE to support clinical trial designs (e.g., large simple trials, pragmatic clinical trials) and observational studies to generate innovative treatment approaches.{9}

Clinical Research Platforms: Connectivity is the Key to Success

The shift to DCTs coupled with the proliferation of digitized health data has elevated the importance of clinical research platforms, which must help administrators and investigators:

- Collect, manage, analyze, and disseminate voluminous patient-reported and physiological data generated by computers, mobile devices, wearables, and other biosensors.

- Establish seamless connections between trial managers, patients, devices, trial data, and information systems.

To accomplish this, a modern research platform ideally should:

- Enable data collection from whatever devices a patient wants to use or allowed by their medical insurance.
- Offer patient-friendly collection tools that allow participants to easily upload and share their data remotely or in the clinic.
- Integrate multiple flows of data and enable investigators to view all patient information through a single portal.
- Provide rich sets of RWD, which can be invaluable for researching a wide range of interventions, variables, and specific patient populations.
- Monitor and measure safety signals (e.g., low blood sugar in diabetes studies) to enable prophylactic or real-time interventions.
- Enhance personalized and continuous patient engagement to improve adherence and data quality.
- Include sophisticated analytical capabilities to provide insights into patient behaviors.

By creating robust research platforms, companies will be able to track, analyze, and share much larger and more diverse datasets from more complex studies.

Conclusion

In an industry that often seems resistant to change, the pandemic has triggered widespread adoption of novel remote monitoring technologies and decentralized approaches. Although still in its early stages, this modernization of clinical trials will continue to be fueled post-COVID-19 by exponential growth in digital health adoption and capabilities. Future clinical trials promise to be increasingly efficient, diverse, and patient-centric while providing researchers with richer, more timely, and more meaningful information.

References

1. Dorn, AV. 2020. COVID-19 and readjusting clinical trials. *The Lancet* 396(10250):523–4. https://doi.org/10.1016/S0140-6736(20)31787-6
2. Carlisle BG. 2021. Clinical Trials Stopped by COVID-19. The Grey Literature. https://covid19.bgcarlisle.com/
3. Clinical Trials Transformation Initiative. Decentralized Clinical Trials. Published September 2018. https://www.ctti-clinicaltrials.org/projects/decentralized-clinical-trials
4. Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards. U.S. Food and Drug Administration. Published March 2020 (Updated January 2021).
5. Ledford H. 2020. The coronavirus outbreak could make it quicker and easier to trial drugs. *Nature* 582(172). https://doi.org/10.1038/d41586-020-01524-0
6. Tufts Center for the Study of Drug Development. 2020. *Tufts CSDD Impact Report*. https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5e303c3dd4520c015cb8a4b1/1580219453985/JanFeb2020_CropSummary.JPG
7. Plana D, Arfe A, Sinha MS. 2020. Re-envisioning clinical trials during the COVID-19 pandemic. *Health Affairs*. https://www.healthaffairs.org/do/10.1377/hblog20200702.963588/full/
8. Klonoff DC. 2020. The New FDA Real-World Evidence Program to Support Development of Drugs and Biologics. Journal of Diabetes Science and Technology.
9. U.S. Food and Drug Administration. 2020. Real-world data (RWD) and real-world evidence (RWE) are playing an increasing role in health care decisions.

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TRIALS & TECHNOLOGY

Radiomics: Why Advanced Imaging Analytics Will Drive More Personalized Drug Development

Rose Higgins
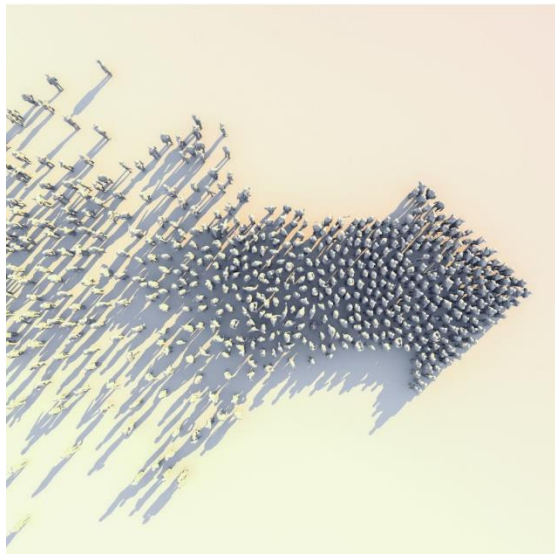
For more than a decade, the concept of personalized medicine has loomed over the healthcare industry with its promise of individually tailored treatments that could deliver better outcomes.

As far back as 2007, a *Harvard Business Review* article clearly laid out what's at stake in the pursuit of a more personalized approach to medicine: "Accelerating the adoption of personalized medicine is enormously important in terms of saving both lives and dollars."

At the time, however, the authors lamented that progress toward this more personalized approach had been "slow and uneven" in the U.S. and across the globe. Now, that may be about to change as the field of radiomics (advanced imaging analytics) is poised to complement existing approaches to personalized medicine to enable drug developers to produce more precise therapeutics.

First, let's back up for a second. When the life sciences industry has traditionally thought about personalized medicine, the concept was based on analyzing genomic features to develop data to quantify a patient's risk of developing a disease—searching for mutations in certain genes that increase a patient's chances of breast cancer, for example.

More recently, advanced imaging analytics, which involve the artificial intelligence–assisted extraction of high-dimensional data from medical images, has emerged as the other side of the personalization coin. Here's how: By coupling a patient's genetic data with his or her radiomics-derived, tumor-specific structural (or phenotypic) data, drug developers can generate therapies for that individual with increased levels of precision.

What is Radiomics and What Can it Do for Drug Developers?

Using traditional and conventional methods, radiologists' views of patients' images and lesions have been limited to only two dimensions – the long and short axes. Consequently, the primary approach to discerning changes to lesions and tumors involved measuring the two axes to evaluate how they change over time. Unfortunately, this approach misses a lot of key information.

In the real world, lesions and tumors possess and are defined by multiple dimensions, in addition to numerous other structural characteristics. Human cancers, for example, demonstrate many phenotypic variations that that can be visualized noninvasively by advanced medical imaging.

For drug developers, radiomic data gathered through the advanced analysis of medical images leads to more precise profiling of patients, tumors and therapies across multiple dimensions, enabling life sciences companies to find patterns and similarities that would be unobtainable through conventional means.

More specifically, coupling patients' radiomic data with their genetic information helps life sciences companies conduct clinical trials with greater accuracy and speed by uncovering insights that cannot be discerned from traditional reading methods of standard imaging modalities such as CT, MRI, or PET scans.

Radiomics can also benefit drug developers by contributing to the "last mile" of personalized medicine development. The combination of genomic data in addition to phenotypic data obtained by radiomics from medical images provides life sciences companies with greater adaptability in clinical trial design by mapping the effectiveness of drugs to show whether treatments under trial are more effective for patients with shared characteristics.

Accelerating Clinical Trials with Advanced Imaging Analytics

The growing popularity of adaptive clinical trials has led to drug developers performing reviews and analyses of results throughout the trial process. For example, whenever researchers surface relevant trial data from laboratory work, imaging, or other sources, they can adapt trials to account for these factors with regulatory approval. As more data are captured and analyzed, the ongoing trial will yield more accurate and precise conclusions.

By showing previously hidden data and patterns within a lesion, radiomic data represent a positive addition to these datasets that serves as an early indicator of treatment effectiveness. For example, linking tumor phenotype and mechanism of action of a novel drug helps developers address tumor aggressiveness, metastatic potential, and tumor response to therapy.

Used in this way, radiomics can accelerate adaptive clinical trials by delivering greater focus. In cases in which advanced imaging data reveal the shared patient characteristic for which a therapy is most effective early in a trial, researchers can center their attention on those patients. Similarly, radiomic data can reveal to life sciences organizations whether the market for a particular drug that appears to benefit only a small subsegment of the target population is significant enough to continue pursuing.

Leveraging Radiomics to Create Better Phase III Outcomes

The transition from Phase II to Phase III of a clinical trial represents a stage of the drug development journey that brings high risks in terms of wasted time and investment. To overcome these risks, researchers can look to radiomic data to obtain a deeper understanding of the shared characteristics of the patient groups for whom the treatment has delivered the greatest and least benefits.

As a result, researchers can then target for clinical trial recruitment patients who share these characteristics—to investigate whether there are even deeper similarities or any barriers within what appears to be the target group that would prevent success. Leveraging this enhanced focus, life sciences organizations gain the ability to reduce overall drug development timelines substantially, while also cutting associated costs and delivering a more precisely targeted treatment to patients.

Conclusion

While the life sciences industry has without a doubt experienced consequential advances in personalized medicine since the "slow and uneven" days of 2007 referred to earlier, few would dispute that we have a lot more progress to achieve. By representing the missing link that connects an individual patient's phenotypic and genomic data, radiomics can help drug developers engineer more targeted, precise therapies that will help deliver on personalized medicine's promise.

Rose Higgins serves as Chief Executive Officer of HealthMyne, a pioneer in applied radiomics, which is the cutting-edge field of extracting novel data and biomarkers from medical images.

OVER THE TRANSOM

Clinical Research's Most Wanted: The Perfect Patient

Gary W. Cramer

"I refuse to join any club that would have me as a member."—Groucho Marx

Taking our cue from the inimitable comedian quoted above, this issue's roundup of excerpts from recent press releases launched into the weboverse by various companies and organizations (no endorsements implied) focuses on the challenge of attracting patients who are perfect for inclusion in a clinical trial but for the fact they don't want to participate, or perhaps more accurately, don't know enough about the opportunity to make a well-informed decision.

Partners Aim to Accelerate Recruitment for Decentralized Clinical Trials

THREAD, a technology and service provider that enables decentralized clinical research, and CureClick, a community-powered platform for participant recruitment for clinical trials, in March announced a new partnership focused on engaging social media influencers to increase recruitment outcomes in decentralized clinical trials (DCTs). Combining THREAD's platform with CureClick's network of more than 100,000 patient activists and advocates, influencers can now highlight potentially life-saving DCTs within targeted social media networks to achieve increased enrollment, retention, and satisfaction rates.

CureClick aims to increase clinical trial awareness and accelerate patient recruitment by enabling trusted members of online communities to easily find and disseminate accurate, patient-friendly information across their social networks. Through this partnership, CureClick patient activists, or "ambassadors," will deliver eligible participants to THREAD's automated participant recruitment and onboarding solution.

CISCRP Announces Second Annual *AWARE for All* 2021 Virtual Event Series

The [Center for Information and Study on Clinical Research Participation](#) (CISCRP), a nonprofit organization dedicated to engaging the public and patients as partners in the clinical research process, in March announced the launch of [*AWARE for All* 2021](#)—a free virtual event series designed to educate the general public about clinical trial research and participation. In the series' second year, CISCRP is hosting five regional events across the country from April through November, with a focus on engaging diverse communities to ensure representative and inclusive clinical research for the future.

Following its opening event for the Northeast region in mid-April, the remaining virtual events in the series are:

- [AWARE for All Northwest](#) (Seattle, Portland, San Francisco, Boise, Billings) on Thursday, May 20, from 4:30 to 6:00 p.m. MDT.
- [AWARE for All Midwest](#) (Chicago, Columbus, Detroit, Indianapolis, Minneapolis) on Thursday, July 22, from 4:30 to 6:00 p.m. CDT.
- [AWARE for All Southwest](#) (Los Angeles, Dallas/Houston, Phoenix, Denver, Las Vegas) on Thursday, October 21, from 4:30 to 6:00 p.m. MST.
- [AWARE for All Southeast](#) (Nashville, Charleston, Atlanta, Charlotte, Jacksonville) on Thursday, November 18, from 4:30 to 6:00 p.m. EST.

Mount Sinai to Lead Team to Decrease Disparities in Cancer Clinical Trials

Mount Sinai researchers [have received](#) a grant award to lead a collaborative team of New York institutions in an initiative that addresses disparities in the participation of Black, indigenous, and people of color (BIPOC) in cancer clinical trials. Stand Up To Cancer® (SU2C) awarded $6 million to a multi-institutional team, its first team of researchers dedicated to health equity in cancer research.

The team, which has been named the SU2C Health Equity Breakthrough Team, will be led by Nina Bickell, MD, MPH, professor of population health science and policy at the Icahn School of Medicine at Mount Sinai. The team includes doctors and scientists specializing in both social

science and clinical research from four New York City institutions that serve some of the most diverse and medically underserved communities in the United States.

"Much of our standard of care in cancer is grounded in research with mostly white populations," said Bickell. "Our goal is to figure out how we can change that—in how scientists approach their work, how medically underserved communities can learn more about pioneering cancer research and treatments, and how care delivery systems can make it easier for patients to learn about clinical trials."

Participation by BIPOC patients in all cancer clinical trials has traditionally been very low. The team will work with community-based groups and community oncologists in New York City to help engage people from medically underserved communities and try to establish new standards regarding their views on cancer care and research, in part by creating a digital system that will link patients with clinical trials in the region.

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