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Mapping the Way to Site Success

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Clinical Researcher—May 2019 (Volume 33, Issue 5)

Table of Contents

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Clinical Researcher—May 2019 (Volume 33, Issue 5)

EXECUTIVE DIRECTOR'S MESSAGE

Thank you, James Lind!

Jim Kremidas

Two hundred and fifty years ago, when the British empire ruled the Atlantic Ocean, Scottish physician James Lind was tasked with finding out why scurvy was killing more sailors than Spanish and French enemies. Like a few others, he had a theory that adding fruit to the military diet might do the trick. For proof, in 1747 he conducted one of the first documented clinical trials.

After eight weeks at sea as surgeon of the HMS *Salisbury*, as scurvy began to take its toll on the crew, Lind decided to test his idea that the putrefaction of the body caused by the disease could be prevented with acids from fruit. On May 20, he divided a dozen sailors into six pairs, and gave each a different supplement in their diet: cider, vitriolic elixir (diluted sulfuric acid), vinegar, sea water, two oranges and a lemon, or a purgative mixture.

As a result of what some have considered the first clinical trial in history, only the two sailors who took the fruit improved. "The most sudden and visible good effects were perceived from the use of oranges and lemons," Lind wrote in 1753 in his historical work *A Treatise of the Scurvy*. "One of those who had taken them being at the end of six days fit for duty … The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick."

We've come a long way since the days of Lind, and while every day is clinical trials day in our industry, we like to call May 20 a special "Clinical Trials Day" and promote its celebration by stakeholders in the clinical research enterprise through events around the country, and the world.

This day of celebration also provides our community with a unique opportunity to raise awareness of clinical trials—and of clinical research as a career option—among the greater public.

This year we are excited to partner with PopUp Star to kick off a contest to bring clinical trials awareness to the masses starting on Clinical Trials Day. From San Antonio to Miami, from Las Vegas to Australia, innovative, and fun, events will educate the public about the value of clinical trials and the work you do every day.

If you'd like to share how you celebrate Clinical Trials Day with us, please check out the ACRP Facebook page at https://www.facebook.com/ACRPDC/ for details as the big day approaches.

Jim Kremidas (jkremidas@acrpnet.org) is Executive Director of ACRP.

Clinical Researcher—May 2019 (Volume 33, Issue 5)

PEER REVIEWED

Three Times the Charm—Transforming Patient Centricity with eConsent, eCOA, and Patient Engagement

Jeff Lee

Imagine seeing a product you want to buy, but when you go to the website, it asks you to print an order form and mail or fax it in. Would you trust that provider or system with your credit card information? Probably not. And yet, that's what we are asking patients to do with something far more important—their health—when it comes to clinical trials. People are used to technology, apps, and accessibility in their daily lives, so it is no surprise that a 2016 survey showed 31% of 137 responding patients reported themselves as more likely to participate in a clinical trial if it has a mobile app.{1}

In fact, Deloitte reports there are more than 260,000 health apps worldwide and the members of 70% of patient groups are using at least one app to manage their condition.{2} By utilizing digital solutions, pharma companies can tap into these progressively health-aware consumers. However, those working in the industry, specifically within clinical trials, often feel that the patients in their studies receive a mixed experience of technology, and many simply feel overwhelmed by too many systems.

So why isn't the pharmaceutical industry moving more quickly to adopt solutions that patients—and sites and study teams—want? Barriers to digitally focused patient centricity include uncertainty over regulators' expectations and requirements, and data safety and privacy concerns with the rise of medical apps and other digital technologies. Such trust issues can result in patients being unwilling to engage with pharma, while low levels of health and digital literacy also affect the ability to engage with patients effectively. Attracting the right talent to support a patient-centric ecosystem can also be a stumbling block, with a traditional product-based culture causing barriers to an agile, patient-centric approach.

Increased willingness to take a patient-centric approach to technology adoption to improve data capture, patient understanding, and patient engagement is needed to drive real return on investment for retention, compliance, protocol adherence, and overall study timelines. The first important step is improving adoption, but equally important is seamless integration and a single, unified user experience for the patient and sites. It is not enough to give them technology—it must blend into their daily lives so that it doesn't get in their way. In other words, we seek easy-to-use solutions built with patients (and how they will actually use the tech) in mind. This article will therefore outline how electronic clinical outcome assessment (eCOA), electronic informed consent (eConsent), and patient engagement apps can work together in one solution to combine to transform the patient experience in clinical trials.

As an aside for readers who are concerned that their patients may lack the technologies necessary for the purposes described in this article, eCOA and eConsent are commonly offered using provisioned devices, so that all patients can utilize them, without regard to their personal mobile phone usage. Patient engagement is typically offered to patients on their personal devices, with either mobile app (for smartphone users) or SMS (text messages) for non-smartphone users.

SMS works on any mobile phone, so this ensures that patient engagement can be provided to virtually any patient.

Creating a Seamless Patient Experience

In clinical studies, it is important to employ approaches that enable the optimal assessment of the study concepts of interest. Where this involves use of a technology solution, the aim is to simplify processes, make participation easier, improve quality, facilitate decision making, and collect reliable, honest data.

Patients and their families are understandably impacted by technology as they are going through a trial. In a typical study, for example, one patient may experience four devices, such as a wearable, a reminder app, eConsent, and an e-Diary. It is not uncommon for a trial participant to also use a payment and reimbursement website, all accessed via different systems and devices. As new technologies emerge, they appear via specialist vendors, so for each software and device, patients have a learning curve, different access points, and compliance requirements. As a result, the patient is faced with a dizzying array of disparate communications, devices, and systems, and if the process is too complex, the patient is more likely to quit the study and deviate off protocol. Seamless integration and a single, unified user experience are again the key to making participation as easy as possible without overburdening the patient. It might seem obvious, but they only need the tools that they need.

Sites today are leaning on technology help desks more than ever in their struggles to provide patients all the training they require. Fortunately, by combining these technologies into a single project delivery team, sites receive streamlined and coherent training, which makes them more effective educators to patients.

However, it is not just the patient who needs to be considered, as technology has an impact from multiple perspectives. Improving the clinical trial experience for all involved is a priority. For study teams, enabling them to see real-time study progress and improve efficiencies is the top priority for managing the complexities of a trial and not adding to it. Transparent, real-time insight is the key here. Meanwhile for management, any solution should improve oversight, efficiencies, and successful outcomes for return on investment.

Less Vendor Focused, More Solution Focused

As mentioned, seamless patient experience requires successful collaboration across many different areas of a trial—outreach, recruitment websites, screening, verification, eConsent, registration, data collection, data return, and incentives. How to bring all these elements together needs to be considered carefully, especially in a virtual trial where there may be no physical site. Figure 1 demonstrates what successful collaboration could look like.

Figure 1: Coordination Among Multiple Systems Sets a Higher Bar for a Seamless Patient Experience

eConsent, eCOA, and patient engagement solutions are the cornerstones of a dependable, patient-centric technology solution to help improve the speed, reliability, and insight of clinical research. Combined into an integrated solution, it makes for a powerful approach.

eConsent

Patients need to be informed and retention starts on the right foot through the informed consent process. eConsent sets the patient up to fully understand the study well, and the engagement aspect carries them forward. eConsent incorporates patient-friendly features such as familiar and convenient mobile devices, multimedia video education, pop-up glossary terms, digestible electronic consent form sections, clearer assessments, and enhanced accessibility (i.e., audio narration, large fonts, etc.). There is a growing body of evidence to support the idea that eConsent improves patient comprehension and study retention. One study{3} demonstrated an increase in assessment understanding with eConsent education; meanwhile, CenterWatch{4} highlighted that it is possible to enroll 25% fewer patients to reach the same completion goals as paper-based studies. In addition, consent-related deviations are the second most common audit findings (e.g., people consenting on the wrong version, not re-consenting to new protocol amendments, etc.). eConsent practically eliminates these deviations and improves compliance, thus delivering major benefits in time and cost at the end of a study.

The benefits also extend to study teams, offering advantages such as real-time consent monitoring, bring-your-own-device (BYOD) implementation, SaaS content system creation (with customers configuring their own programs rather than relying on the platform provider for implementation services), eSignature, print-to-sign functionality, and a fully validated solution that provides value anywhere in the world.

eCOA/ePRO

With patient engagement–focused eCOA and electronic patient-reported outcome (ePRO, in which patient surveys are collected to help assess responses to the therapy that can't be measured by lab tests) technologies, the patient has a better experience within the study, which underpins the ultimate goal of capturing the most reliable data and achieving higher retention rates and improved protocol compliance. Whilst a paper-based option could seem easier for patients to use to record information whenever needed, eCOA forces them to respond *correctly*, with guided

responses, and only during the times specified by the protocol, thus preventing “junk data” from being entered at whim or convenience and misleading sponsors.

Access to reminders about personalized medications, appointments, and other study-specific details, benefiting from a single, mobile touchpoint that integrates study commitments into their daily life, are extras that increase engagement among patients. Content libraries presented in digital form, including video, PDF, audio, images, and text, can also facilitate comprehension and help keep the patient fully informed about the study. Bringing these together is an important way to guide patients through their study experiences—giving them the information they need all in one place. This is crucial in a virtual study, which offers less “hand holding” to patients from the site, making the reliance on technology more important.

Patient Engagement

Engaging a patient on a mobile device may drive better patient outcomes, compliance, change behaviors, etc. In the arena of mobile health, it is obvious that technology is vital, but it is important to look at the tools in terms of the value they deliver. Effective patient engagement solutions should eliminate the need for patients to access multiple disparate systems or rely on manual paper practices to keep up with study requirements. For study teams, mobile programs should be configured to match specific study protocols, work across all smartphones and tablets, and be deployable in a BYOD model.

Such a single, streamlined experience has numerous benefits for all stakeholders, and is a significant aid to making evidence-based decisions. Successful patient engagement apps preferred by patients are ideally integrated into a seamless solution providing a much-simplified experience. They integrate visit reminders, documents, site contact info, critical updates, reimbursements, and courier services (e.g., Uber) into a single app. So even when multiple third-party providers are delivering the services, it is invisible to patients because it is all behind the scenes of the user-friendly app. The aim of technology should be to provide a better patient experience. Increasingly complex protocols are challenging enough without overwhelming technologies, plus a single patient experience inspires confidence in overall study conduct.

A streamlined experience is also simpler for sites, requiring less effort but greater impact. Single sign-on and data sharing across systems fosters simplicity and efficiency for site staff, while centralized data entry reduces the possibility of erroneous data and can reduce operational time and cost. Patient engagement apps also offer advantages for sponsors, as trials run smoothly, with faster recruitment and improved retention. Apps can increase patient comprehension of the study and reduce patient burden, resulting in higher completion rates. Efficiencies for sites translate to more active sites, and faster enrollment and less manual data entry provides better data accuracy and integrity.

In a recent vaccine study, patients were offered the option to receive patient engagement messages on their mobile device. Those who chose to receive SMS reminders, including visit reminders and engagement messages, had a 50% lower drop-out rate than those who did not. This also correlated with higher completion rates in the study, demonstrating a significant opportunity to guide the patient. The added benefit of this technology is that is can be used on both a patient's own device and a provisioned device (BYOD). In a virtual study model, a personal device is more common, making it easy for the patient to download an app.

A First for Patients—Combining ePRO, eConsent, and Engagement

Patient engagement is fundamental not only within a traditional clinical trial setting, but also within a virtual trial, offering a new method of collecting safety and efficacy data from clinical trial participants. Virtual trials (also referred to as direct-to-patient, siteless, or remote trials) are decentralized trials that are less site-centric. The benefits of such trials are that they increase access to include hard-to-reach patient populations (i.e., new geographies) and allow the patient to perform study requirements independently away from the site. Challenges include drug supply, identity verification, consent, and more. Virtual studies are poised to take full advantage of the technologies that are out there, and this is where the value of collaboration and integration really comes into its own.

Case Study—An Integrated Solution

A recently created study sponsored by a top 10 pharmaceutical company looked at developing a deeper understanding and body of evidence around quality of life (QOL) metrics for a specific

indication. There is a lot known about patient experience measured by biomarkers; however, the sponsor believed that the therapy has benefits to the patient that extend beyond optimizing the biomarker measure response. The sponsor wanted to conduct a health-related, QOL virtualized, observational study to attract a large number of patients with this indication and engage with them, with the goal of learning more about their QOL with this indication. Recruitment began in January 2018 with the goal of recruiting up to 1,500 patients. The sponsor was looking for an integrated technology solution to improve patient retention and identity verification. They wanted a solution that increased verification accuracy and reduced patient effort while increasing their comprehension of the study.

The integrated, end-to-end solution for patients was to be a second-generation initiative which presented opportunities and objectives to address challenges experienced in the previous trial, including:

The Challenges

- Patients were quick to join the program, but many did not persist (very high drop-off rates)
- A lack of patient engagement and support through the program
- Sponsor needed a reasonable assurance of each patient's identity/medical condition

Key Requirements

- Take consent to the next level by increasing patients' comprehension of the study
- Do more than collect data
- Improve patient retention
- Be patient friendly
- Follow a similar model to the app store that patients are familiar with to download an app
- Take specific care verifying the patient's medical condition (via disease-specific screening questionnaire)
- Keep the patient's interest through to completion

The Solution

The gold standard approach encompasses digital outreach, patient discovery via a landing page and a study overview section, screening, and eConsent through to an engagement app via the patient's own device, making the process as easy as possible for the patient.

Such a solution offers a much-improved experience to patients and study teams. For patients, it offers a seamless experience, with less work and fewer systems and interfaces, whilst also building trust and increased understanding of the study. Patients are seamlessly guided through the process of learning about a study, understanding their eligibility, consenting, and beginning their engagement through their mobile device. The BYOD diary/patient engagement tool was quickly set up via an automatically initiated activation message sent directly to the patient's phone. An effortless patient activation process takes the burden off sites and patients. Ease of use and rapid patient setup process instills confidence in users, as the system is intuitive even to first-time users. For study teams, this results in faster recruitment and better retention, higher conversion rates, and better diary completion rates. Full launch documentation was provided, including ethics committee/institutional review board (EC/IRB) submissions, data protection statements, and testing documentation, making deployment virtually effortless for the client team.

Despite targeting a niche patient population, the study reached its enrollment goal well before the target "last person in" date and well under the original outreach budget. Completion rates of the consent form suggested a good balance of user experience and rigor of consent form.

Automated study reminders kept patients on track with the protocol and reduced the burden on clinical research sites who would ordinarily remind study subjects to fulfill their commitments to the program. The solution delivered protocol-specific reminders about study medications, appointments, and PRO diary windows, as well as other need-to-know details. These were sent via text message, push notification, e-mail, or voice.

Completion rates (for both the diaries and the overall study experience) were approximately 10 times higher than the predecessor study, significantly exceeding the expectations of the sponsor.

Some Thoughts About Privacy

Our industry is faced with a complex and ever-changing privacy and data security landscape. Each provider of patient-facing technologies approaches these requirements differently, which creates a challenge for all parties involved. Sponsors expend significant effort auditing/qualifying each provider. Sites (and their EC/IRB groups) need to assess and verify that patient privacy rights are upheld by each provider. Patients need to reach a level of comfort with the idea that the multiple technologies with which they are interacting are all safe and secure.

By bringing all of these technologies together, this landscape is greatly simplified for all parties. Additionally, given the scale of providing multiple solutions, a larger organization can more easily stay fully up to speed on changing regulatory frameworks and legal requirements across the many geographic territories in which research is conducted.

A Future-Proof Gold Standard Solution

There is huge potential for thinking differently about how existing technologies can be utilized to enable novel measurements for health outcomes and health status in patients, while making the process as easy as possible for patients to participate in a trial. The goal is to move the industry beyond paper, for its obvious limitations and risks, while navigating the current landscape of decentralized, fragmented systems that do not talk to each other. First and foremost, we need to increase adoption, but just as important is the need to utilize technology in a seamlessly integrated way that fits into patient lives to collect life-changing insights without the trial hindering the process or the patient.

The vision of an integrated system with eConsent, eDiaries, reminder apps, and ePRO in one mobile solution that offers a unified solution—for improved patient experience with increased virtual capabilities—is here, but that is not the end. Novel use of technology encompassing wearable devices, smartphone sensors, and motion-based gaming platforms to collect new endpoints is coming along quickly. A future-proof gold standard solution is available through

best-of-breed collaboration and pioneering solution integration intrinsic to this vision of transforming trials and the patient experience.

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Clinical Researcher—May 2019 (Volume 33, Issue 5)

PEER REVIEWED

Trial Complexity and Coordinator Capacity: The Development of a Complexity Tool

Alexa Richie, DHSc; Dale Gamble, MHSc; Andrea Tavlarides, PhD; Carol Griffin

Assessing the capacity of a clinical research coordinator (CRC) is something that many medical research centers struggle with. Not all studies have the same needs or require the same level of support. What is an appropriate balance of minimal risk versus greater than minimal risk or complex studies? How can the complexity of a clinical trial be assessed in a consistent manner across varying disease types? Research leaders struggle with these questions and how to adequately staff their research units to prevent burnout or decreased quality of services.

Most research positions across institutions are extramurally funded, which presents challenges for not only immediate staffing needs, but makes getting to a state of predictive staffing nearly impossible. Over the last several years, Mayo Clinic Florida has gone through an iterative process to develop and refine a tool with the dual purpose of assessing the complexity of a clinical trial and, by extension, using that complexity assessment to determine the trial capacity of a research coordinator.

Background

The tool is based upon the widely available National Cancer Institute (NCI) complexity assessment,{1} which focuses on the key elements of hematology/oncology trials as they relate to number of study arms, complexity of treatment, data collection complexity, and ancillary studies. These elements were categorized as standard, moderate, or highly complex. The NCI focused primarily on community-based programs, and scored on tasks related to direct patient care interactions.{2}

In our local development process, we wanted a tool with a broad scope so that it could be applied to studies of all diseases and even to non-treatment trials. We used the NCI tool as the foundation, but modified it so that any clinical trial at Mayo Clinic Florida would be assessed for complexity in a consistent manner. Through this process, we were able to score biobanks, registries, expanded access situations, drug trials, and device trials in a uniform fashion.

We considered all stages of running a study to determine overall study complexity. The first iteration of the tool was comprised of 21 unique elements each with a possible score of 0 to 3 points. For example, we included items scored on values such as recruitment strategies, principal investigator (PI) experience, screening procedures, number of visits, numbers of departments involved, frequency of monitoring, and activities at follow-up.

One of the elements assessed is the amount of data that must be collected by the local site. Data collection has a significant impact on how much effort will be required for the trial. A score of 3 would indicate that the data are complex and might need to be entered within three days.

Another example is the amount of time needed to complete a baseline/randomization visit. Minimal effort—a score of 1—would relate to any tasks in the baseline/randomization visit that occurred in less than four hours of total time. Baseline/randomization visits requiring greater than eight hours total time received a maximum score of 3.

Guidelines included in the tool provide instructions for what to do in cases such as when baseline and screening visits occur on the same day (only one value is scored 0 to 3 while the other is marked N/A). Figure 1 details how the scores can be applied to the categories.

Figure 1: Examples of Complexity Tool Categories and the Scoring Matrix

Complexity Tool				
Study Element	**No Effort**	**Minimal Effort (1 point)**	**Moderate Effort (2 points)**	**Maximum Effort (3 points)**
Active Scoring Elements				
PI expertise and experience with clinical research	N/A	Physician has been lead P.I. on several trials and has a clear understanding of a P.I.'s responsibilities	Physician has been Sub -I on a study (ies) and has enrolled and followed patients on a clincial trial	Physician has minimal research experience and/or requires an increased level of engagement
Study Recruitment	N/A	Development of flyers or adding to LCD screens	Community outreach	Specialized recruitment efforts will be required
Target enrollment	0	<20	20 - 100	> 100
Inclusion/ Exclusion Criteria	N/A	1-10 Inclusion/ exclusion criteria	11-20 inclusion/ exclusion criteria	> 21 Inclusion/ exclusion criteria
Informed consent process (initial)	No informed consent	1-10 pages	11-19 pages	> 20 pages
Screening procedures for eligibility (post IFC)	0	1-5	6-10	> 10
Screening visit (length)	N/A	< 4 hours	4-8 hours	Over 8 hours
Randomization/ Baseline Cycle 1 Procedures	0	1-5	6-10	> 10
Baseline visit/ randomization (length)	N/A	< 4 hours	4-8 hours	Over 8 hours
Personnel required other than the research team, Feasibility of the study	N/A	Involves only the research team,	Involves moderate number of different medical disciplines and staff	Involves high number of different medical disciplines and staff, requires more effort and coordination
Procedures needed after Baseline/ Randomization to End of Treatment (outside of procedure/drug)	0	1-10	11-20	> 21

The highest possible score when adding up all 21 items is 63 points. The elements of the complexity tool relate to the overall study design, team engagement, target accrual, consenting processes, length of study, monitoring elements, billing requirements, and whether there are any associated ancillary studies.

The clinic's Research Leadership team held several brainstorming meetings to refine the complexity assessment criteria upon which any study would be evaluated for content validity across cancer, neurology/neuroscience, and general non-cancer trials. These meetings occurred until we could ensure the tool could be applied consistently and comprehensively across all clinical trials. We then tested our tool on current protocols in all specialty disease areas, across Phase I through IV and pilot studies, observational registries or biobanks, and device trials by having multiple team members score a study to determine if they resulted in the same or similar

scores based upon their interpretation of the protocol. Once content validity was established, we were ready to develop a standard for using the Complexity Tool as a predictive work load indicator for trial capacity of a research coordinator.

Developing a Standard

We began validating the tool in early 2017, with the Research Leadership team on the Florida campus scoring all active studies to date through December 2016 (n=~430). Each study received a complexity score. These scores were added to the overall portfolio management tracking tool in use at that time. The portfolio tracker lists studies by PI, Disease Type, and Coordinator, and was used to view the research activity within the disease or investigator's study portfolio at any given time, including studies assigned to a specific research coordinator.

Using the Complexity Tool, the team was then able to review these portfolios to see what the cumulative complexity scores were for a designated group of staff or disease type (see Figure 2). In this versatile method, clinical trial portfolios could be evaluated for overall complexity through various views such as by PI, study coordinator, disease type, non-cancer vs. cancer trial, or clinical department. The scores varied depending on how the data were viewed, which led to further discussions on greater development and use of the tool.

Figure 2: Total Complexity Scores for Team and Designated Staff

Study	Enrollment Status	Lead Coordinator	Complexity Score
Trial 1	Open	CRC 1	42
Trial 2	Open	CRC 1	39
Trial 3	Closed to Enrollment - No Patients on Tx	CRC 1	4
Trial 4	Open	CRC 1	42
Trial 5	Open	CRC 1	48
Trial 6	Open	CRC 1	54
Trial 7	Closed to Enrollment - Has Active Patients	CRC 1	44
Trial 8	Open	CRC 1	50

Trial 9	Open	CRC 1	30
Trial 10	Open	CRC 2	43
Trial 11	Closed to Enrollment - Has Active Patients	CRC 2	43
Trial 12	Open	CRC 2	48
Trial 13	Open	CRC 2	50
Trial 14	Closed to Enrollment - No Patients on Tx	CRC 2	10
Trial 15	Closed to Enrollment - Has Active Patients	CRC 2	42
Trial 16	Closed to Enrollment - Has Active Patients	CRC 2	48
Trial 17	Closed to Enrollment - Has Active Patients	CRC 2	39
		Total Complexity Score for this Team:	**676**
		Total Complexity for CRC 1:	353
		Total Complexity for CRC 2:	323

While at first glance there did not appear to be general logic or break points in the scoring, once the studies were grouped by disease type, there were obvious natural breaks in the scoring that could be used to delineate what could be considered a high-, moderate-, or low-complexity trial. For example, a trial score of 45 or higher on the tool was considered highly complex; scores of 30 to 44 moderately complex; and scores below 30 low in complexity.

Addition of a Step-Down Score

From the initial review and feedback, it was recognized that there are varying stages of work throughout the life cycle of a clinical trial. To accommodate the fluctuating needs or varying effort required, a step-down scoring process was incorporated. The initial score calculated is considered the trial's overall complexity, and its use assumes the study is active and enrolling patients.

The first step-down score is to accurately assess the study needs once a trial closes to accrual. This step accounts for trials that may still have active patients being followed, but are no longer accruing new patients. To determine this first step-down score, the six elements that relate to enrollment and baseline assessments are subtracted from the overall complexity score.

The second step-down score is for trials that have closed to accrual *and* have no patients on active treatment. This score applies to trials that are in long-term follow-up only—for example, those assessing survivorship. To determine this score, only the last four elements in the complexity tool are applied for a total maximum score of 12 points (see Figure 3).

Figure 3: Step-Down Categories

Follow-up (Post End of Treatment) Scoring Elements				
Post-treatment visits in 1st year (follow-up visits after drug administration)	N/A	1-2	3-4	> 4
Post-treatment visits after 1st year	N/A	Once per year	Twice per year	Over twice per year
Frequency of required telephone and non-clinic visits	N/A	Once per year	Twice per year	Over twice per year
Complexity of the follow-up visits (Additional testing at follow-up)	N/A	Vitals, questionaire or survivorship check	Standard of Care tests that may include labs, ECHO, EKG, ect.	Non-standard/ complex testing

Through these three possible steps, a consistent and scalable method for assessing the complexity of any type of trial in a uniform way that accounts for the various stages of the trial was made possible, replicable, and scalable. This step-down score takes into consideration the complexity of each CRC, regardless of whether the study is accruing or only following patients.

Conclusion

In summary, the Research Leadership team was able to develop, test, and implement a complexity assessment that allowed for a uniform review of any clinical trial. Through its implementation, we were able to standardize what is considered highly or moderately complex.

After implementation, it was identified that further analysis could be completed to correlate the complexity score of a study with the workload capacity of a CRC. Further development of the

tool was approved, and results of the next iteration of the Complexity Tool will be discussed in a subsequent publication.

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Clinical Researcher—May 2019 (Volume 33, Issue 5)

SITE STRATEGIES

Welcoming Technology into the World of Clinical Trials

Mark Hanley

Virtual trials are gaining traction across the clinical research industry. With providers like VirTrial, IQVIA, Clinpal, THREAD, and Science 37 forming relationships with big pharmaceutical sponsors and contract research organizations (CROs), it won't be long before your site is approached to participate in a virtual trial, if it hasn't happened already. However, providers are taking various approaches on how they engage with sites, so make sure you understand the differences and align yourself with a provider that supports and values your site's mission.

The core benefits of virtual trials revolve around their ability to streamline visits, add convenience for patients, and ultimately get new medications to market faster. It's no secret that traditional clinical trials often exceed timelines originally proposed by pharma companies and CROs, with the most common challenges being recruitment, engagement, and retention of patients. A solution that helps alleviate these hurdles can be a big win for the industry.

Technology Simplifies the Process

Embracing technology in the clinical trial process can help alleviate several of the difficulties traditionally associated with the process. Two concepts in particular, Time Shifting and Place Shifting, provide numerous benefits.

Time Shifting

One of the key reasons patients drop out of clinical trials is because of the lengthy time commitment required. People have busy lives, and though they may genuinely want to join a trial, other commitments keep them from participating. The introduction of Time Shifting can greatly reduce the time required for participation. By using technology to conduct some of the visits remotely, patients can more easily fit the trial schedule into their daily lives.

Take for instance a working mother whose day is booked from 8 a.m. to 8 p.m. with taking children to school, working a full business day, picking the kids up, and heading home only to make dinner and help with homework. There's little flexibility in her schedule during normal business hours to travel to a study site for a required visit. Technology can provide the option of a brief video chat during her lunch break from her personal cell phone, making the commitment possible.

Place Shifting

Traditionally, trials are run through networks of research sites selected by the sponsor or CRO. Participants are required to travel to those selected sites to participate. This requirement often creates challenges with recruitment, particularly for patients in remote geographies. Even for those who have a flexible schedule, the distance may be too great for them to travel for a trial they are participating in voluntarily.

With the use of virtual clinical trials, the distance barrier is greatly reduced. While patients will need to visit the site in person for some activities, the ability to conduct a portion of visits from their home or work makes the overall commitment more feasible. A virtual visit saves travel time and potential wait time onsite. The patient can simply attend the virtual visit from their personal mobile device from whatever location they choose.

Key Considerations for a Virtual Trial Platform

So we can see how virtual clinical trials can provide a welcome solution to some well-known challenges in clinical research; however, there are some considerations to keep in mind when

incorporating virtual trials. If the overall goal is to improve recruitment, compliance, and retention, the key to rolling out a successful virtual solution is to make the trial process as patient- and site-centric as possible.

In addition to adding flexibility around time and place for visits, it's critical to ensure the technology is easy to use—for both patients and sites. Seek to understand all aspects of a virtual trial provider before getting involved, including:

- **Mobile Device Agnostic—**Some virtual trial providers require the use of vendor-provided devices and expect participants to carry the additional device around with them, as well as learn how to use it efficiently. This adds a new burden to participants rather than reducing it. Look for a solution that is device-agnostic and works on the personal devices that your participants already own and know how to use.
- **Multi-Language Translation—**With an increased focus on adding diversity to trial populations, it may be necessary to communicate with patients in various languages. Find a virtual trial provider that offers translation services and medically certified translators. Ideally, you would want to have the ability for three- or four-way calling to include a caregiver or family member when needed.
- **Seamless Experience—**Most clinical trials will require that some visits be conducted in person at a research site. To ensure a seamless experience for patients, and thorough and comprehensive trial data, it is critical to work with a virtual trial provider whose technology is available to any research site.
- **Some Sites or None?**—Some providers work with only a limited network of sites or focus entirely on "site-less" clinical trials. For example, according to one provider's website, its virtual trials involve no visits to physical trial sites at all.{1} So for your site's sake, be sure to look for a virtual trial provider that understands the necessity for a hybrid approach for trials that require a combination of in-clinic and virtual visits.

Conclusion

Get up to speed on how virtual clinical trials enhance the research process so you're familiar when the time comes to test one. Several providers offer free (and sometimes customized) demos

on their websites. For additional information, you can look for educational resources about virtual trials from industry-related associations, such as the Association for Clinical Research Professionals.

Reference

1. https://www.science37.com/blog/siteless-clinical-trials-changing-the-game-for-patients/

Mark Hanley is CEO of VirTrial.

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GOOD MANAGEMENT PRACTICE

Extracting Scientific and Economic Value from Clinical Remnants

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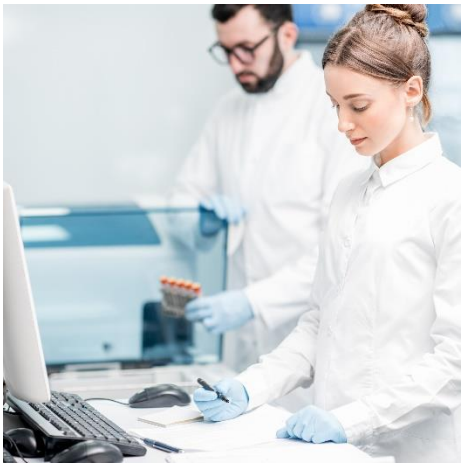

No one likes waste. We close our windows when the AC is on. We invest our savings. We recycle our grocery packaging so the material can be used once again. How, then, can we in the medical community discard untold volumes of human blood, urine, and other biofluid specimens that flow through U.S. clinical labs every year—specimens that researchers desperately need?

We can't. Or at least we shouldn't. Biospecimens for science can be difficult to procure and, as a result, researchers are forced to postpone their vital work on new therapeutics and diagnostics until the appropriate specimens can be acquired. Moreover, in this era of precision medicine, researchers' needs are getting only more specific. Instead of requiring 50 generic blood samples, they may need 50 plasma samples from patients with myeloid leukemia exhibiting a particular analyte over a certain threshold.

Today, however, clinical labs can more easily address this procurement challenge while enabling reuse of their remnant biospecimen samples and earning new revenue—all with limited impact on laboratory operations, thanks to automation at virtually every step.

The Specimen Gap

Historically, when researchers have needed specimens, they have typically relied on phone calls, e-mails, and word of mouth to cobble together their collections. The process hasn't worked too well. In fact, four out of five researchers in one National Cancer Institute study reported limiting the scope of their work because of the difficulty of procuring high-quality samples. In other words, we're slowing research and development progress by discarding viable specimens.

Even biobanks—whose sole purpose is using biospecimens to advance medicine—contribute to the specimen gap by failing to release specimens to researchers. In a recent review of 42 biobanks, 67% cited underutilization of samples as a major or moderate biobank challenge—the most frequently cited of 13 choices.

Most surprising of all, perhaps, is that while vast quantities of human biospecimens flow through clinical laboratories every day, the overwhelming majority are discarded—on average, about a week after testing is complete. It's a virtually untapped stream of material perfectly suited for disease and diagnostic research for the scientific community, and a commonly overlooked opportunity for additional revenue for a healthcare system.

What has been missing from specimen procurement and has led to this specimen waste is an efficient way to match labs' rich source material to the researchers who need it. Specifically, biomedicine needs sophisticated data mining tools to search laboratory and clinical information systems and identify patients and specimens that meet researchers' requirements. Additionally, the process must effectively de-identify and anonymize every specimen and dataset to ensure compliance with the Health Insurance Portability and Accountability Act (HIPAA), the Health Information Technology for Economic and Clinical Health Act (HITECH), and all other regulations that govern the use of patient materials for research and comfortably satisfy the growing level of concern around patient privacy.

A Role for the Internet

The specimen-sharing problem, whether centered on biobanks or clinical labs, stems in large part from this major technical disconnect between the organizations that have such samples and the organizations that need them. The specimen gap has historically resembled the pre-internet book-buying gap between publishers and readers, the flight-reservation gap between airlines and travelers, or the romance gap between compatible singles.

While these gaps have been elegantly filled by Amazon, Kayak, and Match.com, the specimen gap is just now being addressed with new online marketplace technology. This new marketplace enables clinical labs, biobanks, and other healthcare organizations to publish their holdings and researchers to search for the specimens they need. The goal is to accelerate medical progress and eliminate researchers' struggles to cobble together high-quality, data-rich biospecimens for their research programs.

As a side benefit, hospital and clinical lab partners are finally able to make profitable use of clinical material they would otherwise discard—a benefit for laboratories seeking to grow their revenue stream to offset decreasing reimbursement rates.

How the Marketplace Works

The first marketplace to connect researchers and specimen suppliers is just over one year old and has hosted thousands of searches across 25 million samples. The iSpecimen® Marketplace provides commercial and hospital labs with software that monitors the flow of specimens and associated datasets through their sites. The software matches specimens that are about to be discarded to requests made by medical researchers for tissue, blood, plasma, serum, urine, and other fluid/sample types. When a match is made, the software instructs lab personnel to pick, process, pack, and ship the specimens to researchers.

The software also de-identifies the data in accordance with HIPAA. It removes all elements of Protected Health Information (PHI) prior to sending it to the marketplace. PHI never leaves the lab. When an order is placed for specimens the lab possesses, the same software re-identifies the specimens for the lab tech who will pick and ship the specimens.

How to Get Started

The next question is, if you have specimens to share, how would you get on the marketplace and start processing orders? Getting started will depend on your lab technology.

If a lab is automated…

Labs can use the Atellica® Data Manager and the Aptio® Automation system to make their samples searchable by researchers using the iSpecimen Marketplace, and to automate the retrieval of samples requested by those researchers.

If a lab has an LIS or LMS…

For a lab with a laboratory information system (LIS) or laboratory management system (LMS), the process is still streamlined. The lab's specimen inventory is automatically shared with the marketplace via an HL7 feed exported from the lab's software. Using simple checkboxes, the lab can control what inventory is visible to marketplace users.

The marketplace's software guides lab techs through the entire process to ensure the correct specimens are shipped to the right researcher. This integration, which entails some collaboration between the information technology (IT) teams of both the lab and marketplace, accelerates data exchange, reduces supplier tasks, and minimizes the chance of clerical error.

If spreadsheets are used to manage specimens…

For the rare lab without a dedicated LIS or LMS, staffers send spreadsheets of specimens and data to the marketplace operator to offer available samples. iSpecimen's team manually imports the data into the marketplace's specimen database—a process that can take up to a few days. When researchers on the marketplace order a set of specimens that match the lab's supply, the marketplace automatically creates a picklist for the supplying lab.

Just a Normal Marketplace Onboarding

As with any marketplace, it takes an initial action to get on board—typically a meeting or two with the marketplace provider. How easy it is to participate depends on a laboratory's IT capabilities. If a laboratory is already automated, participation is simple and productive. Manual sample management will require additional steps.

The advent of this marketplace enables a compliant, reliable, and virtually automated way for labs to contribute specimens to researchers. Imagine the benefits virtually unlimited access to specimens could have on research and development, and the opportunities this offering provides laboratories to reduce specimen waste while creating a new revenue stream.

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