

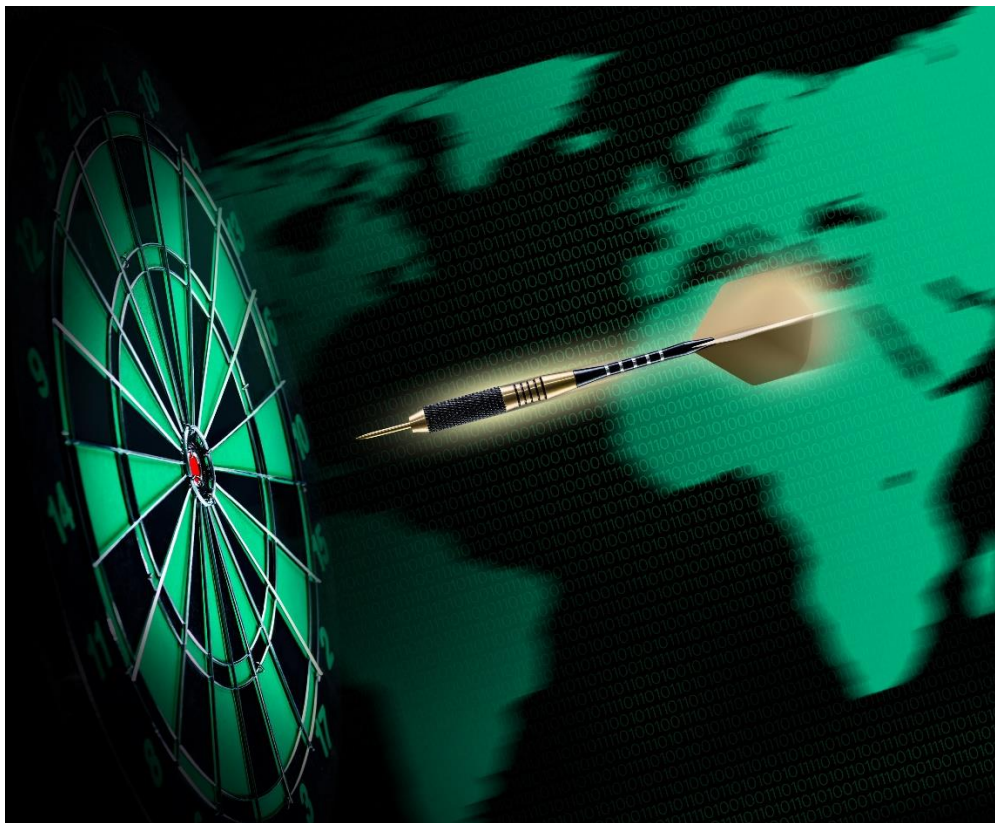


■ FOR LEARNING ■ FOR LISTENING ■ FOR LIFE

Clinical Researcher™

The Authority in Ethical, Responsible Clinical Research

April 2020 (Volume 34, Issue 4)



Aiming for Accuracy in the World of Subject Recruitment

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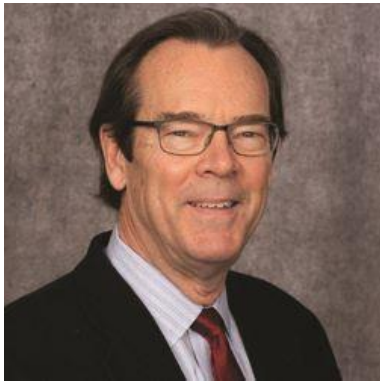


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EXECUTIVE DIRECTOR'S MESSAGE

Learning to Shine When Failure is Not an Option

Jim Kremidas



Faced with one of the biggest potential disasters in the history of the U.S. manned space program to the moon, NASA Flight Director Gene Kranz memorably said failure was not an option when considering ways to rescue three astronauts floundering in space. In Ron Howard's *Apollo 13* movie, Kranz goes further, saying the time of crisis will in fact be NASA's finest hour.

I watched that classic 1995 film recently. Kranz's courage and optimism resonate even more today as we struggle together to adapt to a new normal involving terms like "social distancing" and "flattening the curve," and grappling with a healthcare crisis of an almost unimaginable magnitude. Indeed, our lives have been disrupted to their very core.

ACRP members and other clinical trial practitioners are taking offensive action in this new war against a new foe: the coronavirus causing cases of COVID-19 that are already overwhelming hospitals and other healthcare facilities around the globe.

Speaking on behalf of the team here at ACRP, we've never been prouder to support your vital work protecting health and improving quality of life. In critical ways, you and your work are the ammunition for our key weapon to mitigate the virus today. You are the professionals providing the data and other information needed for front line healthcare workers to help patients in need. Additionally, your work will help us to be prepared to meet the next pandemic in whatever form it takes. It is clinical research that will find the cures we need to win the battle against this deadly virus and future ones.

The work you do is so incredibly important. You aren't doing it for credit or glory, but the fact remains: You are answering a higher calling by working to help advance human health. Now more than ever.

Let's Get Virtual

As you probably are already aware, we had to cancel our physical conference in Seattle, which had been scheduled to begin May 1. The cancellation joined a long list of events of all stripes that continues to grow as we and the entire globe wait to see how damaging COVID-19 will prove to be.

We share your disappointment. The conference is an educational and inspiring time, and we were all looking forward to it very much. Fortunately, starting April 16, we're bringing you the ACRP 2020 annual conference virtually. Our new program includes 25 expert-led sessions across six educational tracks and provides the opportunity to earn up to 24 ACRP Contact Hours.

While we won't have the same chance to network face-to-face over coffee and other beverages, I'm glad you will still have an opportunity to earn credits, swap stories, share best practices with peers, and otherwise commiserate with other leaders in the clinical trial world virtually. I hope you'll be able to participate. [View program details at 2020.acrpnet.org](https://2020.acrpnet.org).

No Spoilers

Finally, for those who haven't seen the movie, I won't spoil *Apollo 13*. Suffice to say, Kranz's dedication and optimism don't go unrewarded.

I see Kranz's steely, resolute spirit in so many clinical trial professionals today. All around the globe, whether it's helping complicated COVID-19 trials launch in a matter of days, or staffing pop-up testing facilities literally under battlefield conditions, ACRP members and other clinical trial professionals are already demonstrating that this is *your* finest hour. On behalf of my ACRP colleagues, I thank you and I salute you.

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

CHAIR'S MESSAGE

Rolling with the Punches, Virtually Speaking

Paul Evans, PhD



It's an understatement to say we are living in challenging times. The COVID-19 pandemic continues to wreak havoc on much of the world as it forces us to change our habits, alter our daily lives, and do our best to prepare for the unpredictable.

In his April message elsewhere in this issue of *Clinical Researcher*, ACRP Executive Director Jim Kremidas rightly applauds and salutes clinical trial practitioners and their vital role battling the coronavirus and other health threats. I couldn't agree more with his sentiments.

However, I wanted to use my space here this month to focus on somewhat more pragmatic matters; specifically, COVID-19's impact on your Association and the broader clinical research enterprise.

For obvious reasons, we were forced to cancel the ACRP 2020 gathering in Seattle. I'm not going to sugarcoat the reality: The financial impact on ACRP won't be small. Each year, the conference and exposition form an important source of revenue for your Association. The education and networking event is a pillar of our operations. Now it's gone.

However, we've come up with a way to make the best of a difficult situation. By now you may have received an e-mail from ACRP outlining how paid attendees can get a voucher for \$150 over the originally planned conference's registration fee. You can use that voucher in a number of ways to both support and benefit from your Association via other training and conference offerings, among other options. I hope you'll consider taking advantage of this exciting offer.

I'd like to applaud ACRP staff for the incredible work they've done taking much of the best of our physical conference and transforming it into the Virtual ACRP 2020 Program, with 25 expert-led sessions, six educational tracks, and 24 contact hours available from activities starting in mid-April and stretching into late June. [View program details at 2020.acrpnet.org](https://2020.acrpnet.org).

As we all grow increasingly stir crazy in the coming weeks, I can't think of a more productive way to use screen time than participating in the Virtual Program.

Our Shared Struggle

It's also important to remember that, as an industry and as an Association, we're going to get through this pandemic crisis and its upheaval. I'd like to strike an optimistic note here and talk a little about ACRP's upcoming physical regional conferences—tentatively scheduled in Philadelphia (September 16–18) and in North Carolina's Research Triangle Park area (September 30–October 2)—each offering an afternoon workshop on the first day and 12 contact hours from full days of sessions on the next two days.

For those undergoing conference “withdrawal” after our Seattle cancellation, these two regional gatherings offer an opportunity to reconnect with colleagues the old-fashioned way! We are also looking at the prospect of adding a few more regional conferences toward the end of 2020. Watch this space for updates.

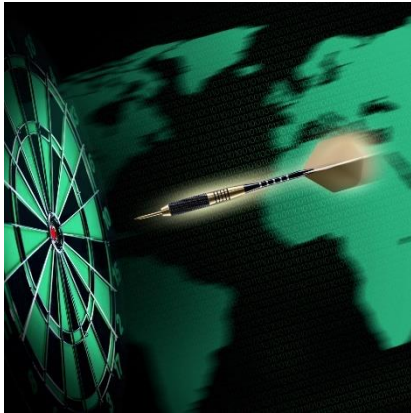
There's an expression that “out of chaos, comes opportunity.” Well, as we think about meetings in 2020, I see an opportunity to revitalize our annual business meeting, too. It's typically held at the annual conference. Let's be candid: Turnout tends to be underwhelming. However, I think we can find a way to do a virtual version this year with more attendees and more interaction. Again, watch this space for updates.

Finally, I'd like to echo Jim's comments and say how proud I am to be working with such a fine group of people sharing such worthy goals. We're in this together, and we're going to emerge all the stronger for it on the other side.

Paul Evans, PhD, is President and CEO of Velocity Clinical Research, and Chair of the Association Board of Trustees for ACRP in 2020.

Aiming for Accuracy in the World of Subject Recruitment

Gary W. Cramer



Recruiting volunteers to do something for which they know they are well qualified and actually have an interest is one thing; recruiting them to do something they don't know they may be ideal for and have maybe never even heard of is quite another matter.

Such is the common dilemma faced by the professionals whose job it is to find volunteers for clinical trials. Finding subjects for Phase I studies offering remuneration is not such a great challenge in most cases, but finding and educating subjects who are actually affected by the conditions under study for later phases of research presents all sorts of stumbling blocks on the way to “closing the deal” and enrolling them.

While gathering and editing the various articles on patient recruitment and retention topics found elsewhere in this issue, I found myself wondering what some of those complicating factors might look like in the real world and asked a few questions. Here are some of those questions and the answers that presented themselves:

Are there country-specific quirks or challenges to be encountered when recruiting subjects—things new recruiters aren't necessarily expecting to be an issue that may suddenly crop up as a hurdle to attracting participants in one or a few countries, but not in others? If so, how have recruiters dealt with them?

According to Tricia Barrett, senior vice president and managing director with [Praxis](#), an industry-leading patient recruitment and retention company, “When creating educational and

awareness materials for direct-to-patient outreach, it's not a one size fits all approach in extending globally. Each country has its own unique rules and regulations, and even more important is the cultural adaptation that must take place—whether it's through imagery, content, tone, or even design.”

Barrett notes that a word or a color can mean one thing in one country and something completely different in another. Further, “A simple language translation is not enough,” she explains. “Transcreation—also known as cultural adaptation—is imperative to a successful global clinical trial. This process ensures that your message is maintained in style, tone, and context.”

Thus, it is important to consult with local experts in the country of focus, or to hire someone who knows the culture to review trial materials before they reach sites and patients, Barrett says. “The same goes for your communications tactics,” she adds. “Be sure you have someone who understands the culture and can perform quality control before you launch any public communications.”

As an example, when Praxis considers names for a study, a list of the favorites is sent to transcreation experts for review. “We were recently working on a mental health study, and one of our proposed study names was the ‘Asana Study,’” Barrett says. “The study was recruiting patients in 12 countries, and while that name had no negative connotation in most, in Hungary, we were informed that the word might be misused by adding a ‘b’ at the beginning and a ‘z’ in the middle (as in ‘baszana’), which [would turn it into] a curse word in Hungarian.”

For best practices in more effectively targeting and engaging study participants, see the Special Features on “Getting Started with Using Social Media to Recruit Research Participants” and “Applying Behavior Change Strategies to Patient Engagement in Clinical Research” in this issue.

There’s been a big drive toward simplifying trial participation (for example, by decreasing the demands for so many visits to sites) and broadening access for study volunteers—one that’s only becoming more urgent in the midst of the coronavirus crisis. What kind of progress is being made on these fronts?

Technology advances certainly appear to be making headway in this arena, with study managers taking advantage of the ever-greater levels of connectivity now possible with their participants. For example, Science 37, a company with a focus on decentralized clinical trials, recently announced that it “has created a fully reimagined patient experience while introducing native support for iOS and Android operating systems. With this development, patients can not only participate from the comfort of their own home, but they can also do it with the familiarity of their own smartphones.”

Using their own devices, patients can learn more about a study, provide consent, schedule and participate in study visits, complete assessments, and communicate directly with the study team and investigators, all through a single platform, according to the company. The cloud-based platform is also touted as integrating workflow and processes for physician investigators, mobile nurses, and coordinators across the entire trial life cycle.

Meanwhile, Medable Inc., a software provider for decentralized clinical trials, recently announced the launch of its Patient Advisory Council (PAC)—a nationwide network of advocates who will advise Medable and its biopharma customers on ways to improve patient access, experience, and outcomes in clinical trials.

According to the company, the PAC “is a network of expert patient advocates, advisors, and caregivers with diverse backgrounds in patient engagement and a strong understanding of patient preferences. The patient-led council is dedicated to improving clinical trial access and efficiency by embedding patient voices and perspectives into every facet of clinical trials, with the goal of bringing innovative, life-improving therapies to more patients at a faster pace.”

Medable further plans to share patient insights with key stakeholders, including healthcare providers, biopharma companies, and clinical research organizations. Original PAC member and past ACRP annual conference speaker T.J. Sharpe, a melanoma cancer survivor and patient advocate, has been working closely with the company to develop the framework, initial guidelines, and best practices for how Medable can best incorporate the patient perspective; patient advocate and founder of One Rare Jennifer McNary serves as the PAC Chair for 2020.

“By giving patients and caregivers a much-needed voice in trial design and execution, life science companies can improve patient access, experience, and outcomes,” said Dr. Michelle Longmire, CEO and co-founder of Medable. “This is a unique opportunity for key stakeholders across the clinical trial landscape to work together and contribute their insights and experience to accelerate innovation. By integrating patient perspectives within our digital trials platform, we hope to offer patients a more human experience.”

From [another announcement](#), this one made at the recent SCOPE 2020 Summit, we also know that Greenphire has teamed up with Roche to address the top hurdles patients face when participating in clinical trials. According to on-the-scene reporting, the companies co-presented findings from a recent global trial survey on patient convenience, highlighting the need to alleviate financial and logistical burdens from participants in order to maximize retention and engagement.

For other views on simplifying and enriching trial experiences for participants, see the “Science & Society” column on “Decentralized Clinical Trials: A Much-Needed Plan for a More Reliable Future” and the “Recruitment & Retention” column on “How to Recruit, Cultivate, and Grow a Clinical Trial Subject” in this issue.

Another aspect of subject recruitment and retention that has become an ongoing emphasis from many quarters of the enterprise is that of diversity among participants. What are stakeholders doing now to improve the involvement of underserved populations in clinical trials?

As just one example of how this situation is being addressed, [a recent blog post](#) from Clinical Research Pathways looked at how multiple sclerosis (MS), “an unpredictable, potentially disabling disease of the central nervous system...has long been viewed as a disease of white women of northern European ancestry, [but] also affects black, Latino, and Hispanic Americans.”

Researchers’ understanding of how common MS is among these populations won’t improve unless more minority patients are included in MS studies. During Multiple Sclerosis Awareness

Month in March, Clinical Research Pathways shined “a spotlight on this disease and the need to increase minority participation in MS research,” noting that, “[if] we understand how the disease affects people of different races and ethnicities, we can develop treatments that work better for all MS patients.”

However, the blog points out, “Black and Hispanic Americans...face obstacles to treatment. One study found that these patients are less likely than white patients to receive care for conditions, including MS, in a neurologist’s office. Without this care, many minority patients end up in hospital emergency departments with more serious problems.”

Clinical Research Pathways encourages healthcare providers, researchers, patient advocacy organizations, and other members of the MS community to learn more about the [MS Minority Research Engagement Partnership Network](#) and take advantage of its engagement resources and toolkits.

For more insights on diversity in clinical trials, see the “Site Strategies” column on “Fostering More Diverse Trials Through Targeted Protocols and Other Tactics” in this issue.



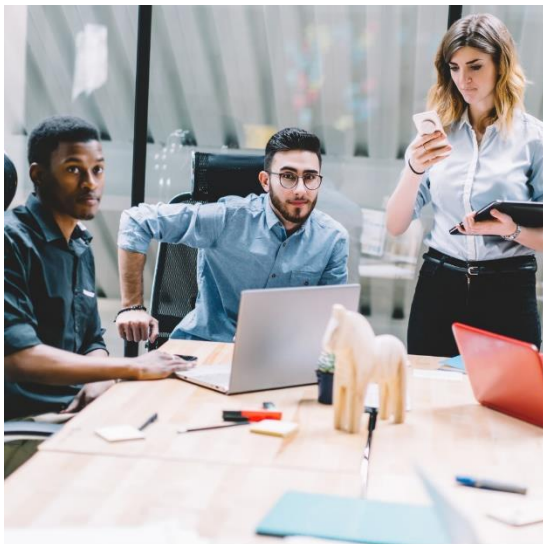
Gary W. Cramer (gcramer@acrpnet.org) is Managing Editor for ACRP.

Clinical Researcher—April 2020 (Volume 34, Issue 4)

PEER REVIEWED

Adapting Productivity Models to Improve Efficiency and Progress in Clinical Research Practice

Kara Lorduy, PhD, CCRP; Victoria Brown, PhD, MBA, CIP, CCRP;
Suzanne J. Rose, MS, PhD, CCRC



According to a recent report on “U.S. Investments in Medical and Health Research and Development,” the biopharmaceutical industry spent approximately \$15 billion in direct costs in the establishment of roughly 4,500 clinical trials in the United States in 2017. These sponsored trials included more than 920,000 participants.^{1} Considering that 86% of trials in the United States fail to enroll before the contracted period,^{2–4} a research program’s stewardship of qualified and well-trained study coordinators, who are tasked with balancing ever-increasing regulatory demands and protocol complexity,^{5} is paramount to its success.

This paper surveys the current state of the field and compares two similar adaptations of the Ontario Protocol Assessment Level (OPAL) in tracking productivity at their respective research programs. {6} The findings provide a compelling case for improved efficiency and productivity, increased job satisfaction and retention, and higher levels of funding over prolonged use of adaptive productivity metrics.

Background

It is well known that coordinating a successful research program has become very challenging in today's clinical research environment, due in part to greater protocol complexity, fewer available studies, decreasing site budgets, high levels of staff burn-out, and an increased regulatory burden. {7} In addition, research sites are often expected to project staffing needs in order to bring on new trials, maintain existing ones, and stay abreast of the regulatory demands for multiple studies. In order to manage the workload of these studies, there is a need to better understand the time, personnel, and financial resources needed to conduct clinical trials. The benefits of this focus include increased enrollment success, funding, efficiency, quality, and job satisfaction and retention of study coordinators.

Historically, federally funded research programs have been guided by the 1992 National Cancer Institute (NCI) Cancer Clinical Investigations Review Committee algorithm of 1.0 full-time equivalents per 40 enrollments. {8} However, meta analyses across 51 research programs alongside many other pivotal developments in this arena, {4} have led to a growing consensus that productivity models should incorporate complexity, or acuity, as well as the regulatory and administrative tasks in their metrics. {9,10}

Recent attempts have been made by various groups and sites to develop workload tools that adequately address the true workload of clinical research coordinators (CRCs). The tools formulate the workload effort through various mathematical calculations. {9,11–17} In an effort to portray the evolution of efficiency in clinical research practice, we depict the replication of the OPAL {6} metrics on improved efficiency at one site (Children's Health System of Texas) following one year of implementation productivity metrics, while another site (Stamford Health)

presents the compounding benefits of adapting the OPAL protocol acuity rating metrics to comprehensively include additional workload factors, coordinator roles, and phases of the study cycle in the Clinical Research Workload Tool (CRWT) across eight years.

OPAL and the CRWT overlap in terms of using an eight-point protocol score, or multiplier toward the total enrollment number, with simple studies (e.g., registries) rating “1” and complex studies (e.g., Phase I) rating “8.” Comprehensively, the CRWT model adjusts the protocol score considering the study role contributions (i.e., data, regulatory, nurse, and coordinator) and adds weights to the score for each additional workload factor (e.g., industry trials, duration or number of visits){18} to comprise a CRWT score or multiplier toward total number of active enrollments before adjusting for the phase of the study (e.g., start-up, enrolling, follow-up).

Importantly, our findings support the growing body of knowledge regarding the adaptation of metrics originally explored in oncology research programs for use in these two non-oncology research programs at two distinct phases in their development of adapting OPAL-based metrics. The non-oncology programs aimed to develop a common currency of productivity that could be benchmarked and leveraged to improve efficiency and progress in their clinical research practice.

Methods

To reiterate, we present two research programs utilizing an adaptation of the OPAL productivity metrics. The first site, Stamford Health, collects data relational to use of the CRWT model across eight years. The second site, Children’s Health System of Texas, collects data relational to use of another adaptation of the OPAL metrics in the first year of implementation.

Stamford Health

The CRWT was developed based on the OPAL workload planning tool.{6} Stamford’s model also allowed for an “other” category, which was determined at the site level for an extenuating circumstance that added protocol complexity. With the addition of the complexity modifications, the total CRWT score could amount to as high as 12.

In addition, another novelty the CRWT accounts for is that, at Stamford, regulatory coordination and data management tasks are assigned to other personnel than CRCs. To account for the regulatory and data management burden not being part of the typical CRC's daily workload, the CRWT offers additional reductions in workload by 25% per additional resource based on a previous workload study in which coordinators recorded their time spent on protocol management, eligibility, and entry, treatment, follow-up, and final stage. Approximately 25% of clinical research associate (study monitor from a sponsor or contract research organization) time recorded was spent on protocol management (regulatory coordinator responsibilities) and 25% of time on follow-up and final stage (data manager responsibilities).{ 19 }

Data were collected over an eight-year period. CRWT scores for 14 coordinators were recorded on a monthly basis. A total of 606 CRWT scores were calculated in this time period ($M=117$, $SD=57.47$).

Children's Health System of Texas

In a similar adaptation of OPAL, the enrollment-derived productivity of a separate, non-oncology clinical research program in the first year of implementation (T1=January 2017; T2=January 2018). Consistent with the methodology defined previously,{ 6 } all protocols included in the research program's portfolio were scored. Children's Health then examined the workload of 10 experienced CRCs. The total workload (the DEVO score) for each coordinator was constituted by two components: 1) enrollment derived productivity using the OPAL (i.e., the OPAL score) appraised workload method{ 9 } and 2) all contributions made to the developmental department initiatives (the DEV score) including, but not limited to, writing standard operating procedures, internal quality reviews, and training (see Figures 6 and 7).

The DEV scores were computed by adding additional points to overall workload score by counting the total number of hours spent across four primary categories (regulatory, training, developmental, and patient care) reported in a time tracking system and dividing them by a factor of two. Additionally, coordinators completed a five-point Likert scale assessing their perceived fairness of the metrics system, as well as how likely they were to "still be working at the department two years from now" and their overall job satisfaction.

Results

Study Conducted at Stamford Health

Figure 1 shows characteristic CRWT monthly score profiles over a four-year period for two full-time oncology (CRC 2 and CRC 3) and three non-oncology (CRC 1, CRC 4, and CRC 5) coordinators who worked four years contiguously.

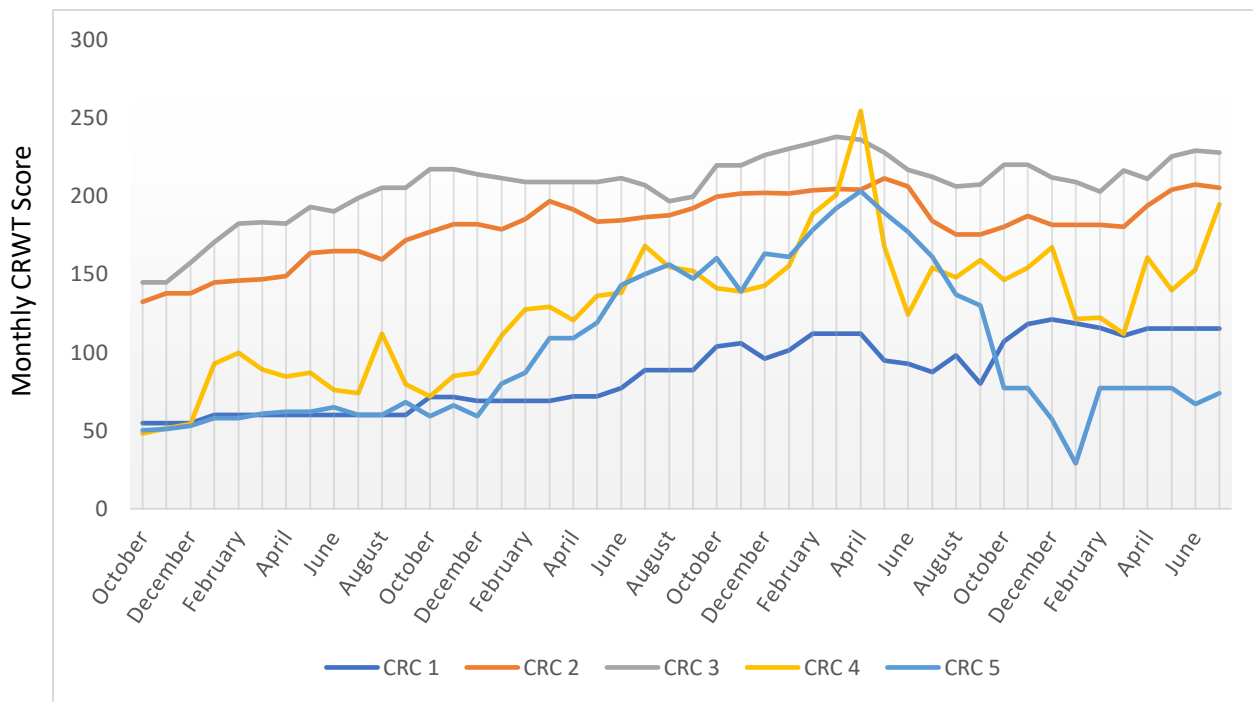


Figure 1: Workload is highly variable among full-time oncology and non-oncology coordinators.

Oncology coordinators average a higher workload ($M=193.5$, $SD=17.78$) than non-oncology coordinators ($M=104.5$, $SD=36.13$). The difference in means was highly significant by a t -test for two independent groups, $t(45)=-10.13$, $p<.001$. This can be attributed in part to the higher number of trials that oncology coordinators ($M=19.25$, $SD=1.86$) conduct versus non-oncology coordinators ($M=8.14$, $SD=4.06$). The difference in means was highly significant by a t -test for two independent groups, $t(45)=-11.34$, $p<.001$.

Based on frequent coordinator assessment of their workload (too light, moderate, heavy, or unbearable) and capability of conducting assigned studies (yes, somewhat, no), four categories were assigned (see Table 1).

Assigned Study Coordinator Ranges

Range	Zone
<100–125	light green
126–150	Green
151–175	Orange
175–200+	Red

Table 1: Coordinators in the light green zone were usually new research coordinators. Coordinators in the green and orange zones were more confident with workload and most capable of taking on new studies. Coordinators in the red zone often felt overworked.

In addition to calculating monthly CRWT numbers, annual revenue productivity per coordinator was calculated and adjusted according to whether the coordinator left the institution. A scatter plot of annual revenue and average annual workload was created, and Pearson’s Correlational analyses were used to examine the relationship between the annual revenue and average annual workload (see Figure 2).

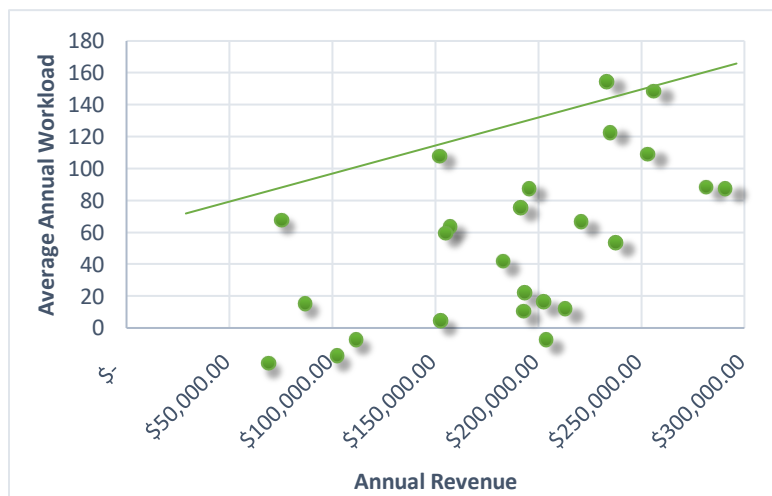


Figure 2: For non-oncology coordinators, a higher workload correlated to greater revenue generation. There was a strong statistically significant positive correlation between average annual workload ($M=104$, $SD=36.13$) and annual revenue ($M=\$121,697$; $SD=\$63,681$), $r=.62$, $p<.001$, $n=27$.

The positive correlation does not appear to be related to variation in study characteristics, as they did not vary greatly during the eight-year period, as shown in Table 2. Studies are categorized as Device (Pre- and Post-Market as well as total Device), Drug (Phases I–IV) and Registry trials not categorized as Phase IV trials. As evident in the data, Stamford focuses primarily (in order) on Phase III drug trials, Pre-Market device studies, and Registry-type trials.

Table 2: Study Characteristics for Non-Oncology Enrolling Trials

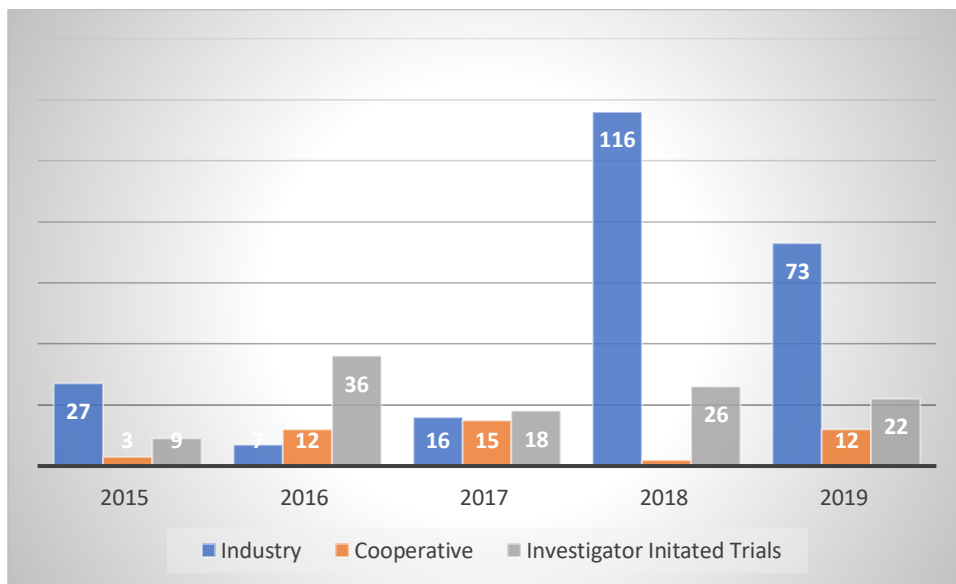
Study Type	N	Mean	SD
<i>Total Device</i>	8	6.50	1.60
Pre-Market	8	5.13	0.83
Post-Market	8	1.88	0.64
<i>Total Drug</i>	8	9.88	4.76
Phase I	8	0.63	0.74
Phase II	8	1.38	1.51
Phase III	8	7.88	3.64
Phase IV	8	0	0
<i>Registry</i>	8	3.25	1.83

For oncology coordinators, a scatter plot of annual revenue and average annual workload was created, and Pearson’s Correlational analyses were used to examine the relationship between the annual revenue and average annual workload (see Figure 3). This was despite a dramatic increase in the number of subjects accrued to industry-sponsored trials in the last two years (see Figure 4).



Figure 3: For oncology coordinators, a higher workload negatively correlated to revenue. There was a strong statistically significant negative correlation between average annual workload ($M=196$, $SD=15.4$) and annual revenue ($M=\$106,094$; $SD=\$49,588$), $r=-.71$, $p<.001$, $n=20$.

Figure 4: Enrollment for Oncology Coordinators by Trial Type



For all coordinators, no correlation was found between average annual workload ($M=142$, $SD=53.36$) and annual revenue ($M=\$115,057$; $SD=\$58,039$), $r=.065$, $p=.666$, $n=47$ (data not shown).

Study Conducted at Children's Health System of Texas

Two-sample, paired t -tests were conducted to test the hypothesis that tracking productivity would improve the efficiency of a clinical research program's enrollment-derived productivity over the course of a year (T1=January 2017; T2=January 2018) holding total coordinator hours worked constant (see Figure 5). Additionally, we tested the effectiveness of our productivity tracking metrics to improve study coordinator efficiency, using two-sample, paired t -tests to compare mean percentages of study coordinator time spent for non-enrollment derived activities (regulatory, training, departmental initiatives, patient-facing) at two distinct time points (T1; T2) holding total coordinator hours worked constant (see Figure 6).

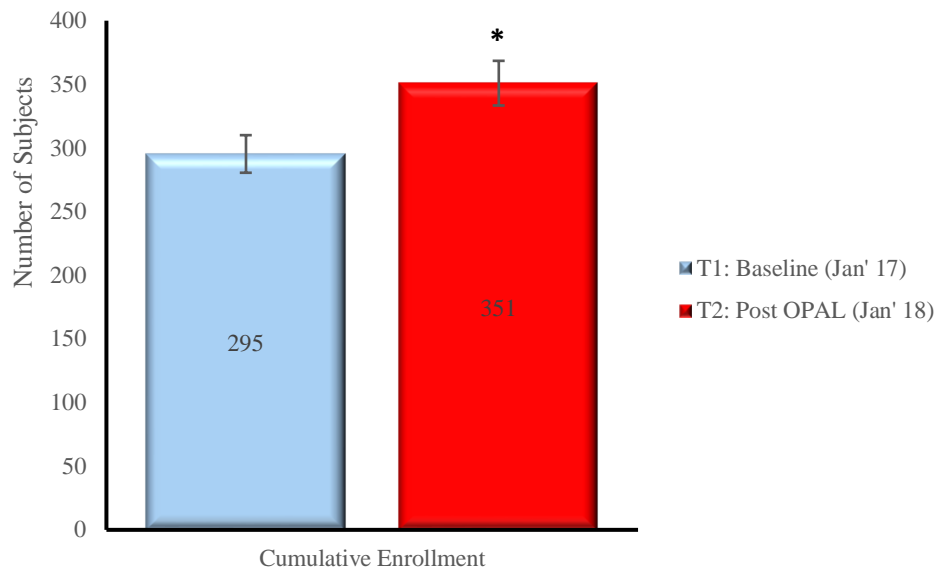


Figure 5: Total cumulative enrollment was significantly increased from T1($M=295.30$, $SE=135.79$) to T2($M=350.90$, $SE=151.49$), $t(9)=-2.80$, $p<.01$.

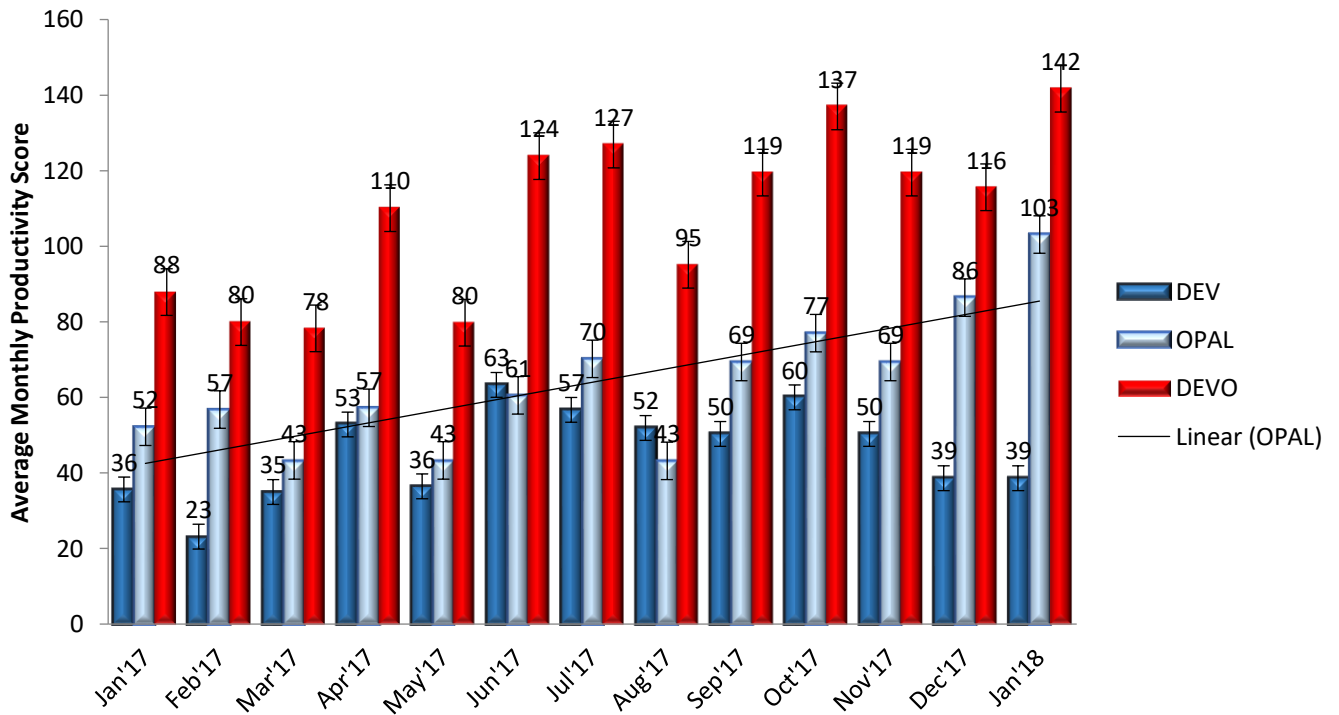


Figure 6: Mean monthly productivity scores significantly increased in enrollment-derived productivity (OPAL) from T1(M=52.23, SE=10.60) to T2(M=103.10, SE=24.98), $t(9)=-2.35$, $p=.02$, demonstrating increased productivity over time as expected. As expected, overall productivity (DEVO), including enrollment-derived productivity (OPAL) and developmental activities (DEV), significantly increased from T1(M=87.86, SE=11.49) to T2(M=141.70, SE=22.79), $t(9)=-2.37$, $p=.02$.

Together, these results demonstrate that increases in enrollment-derived activity coincided with significant increases in the mean percentage of time study coordinators spent in patient-facing activities in the first year (see Figure 7).

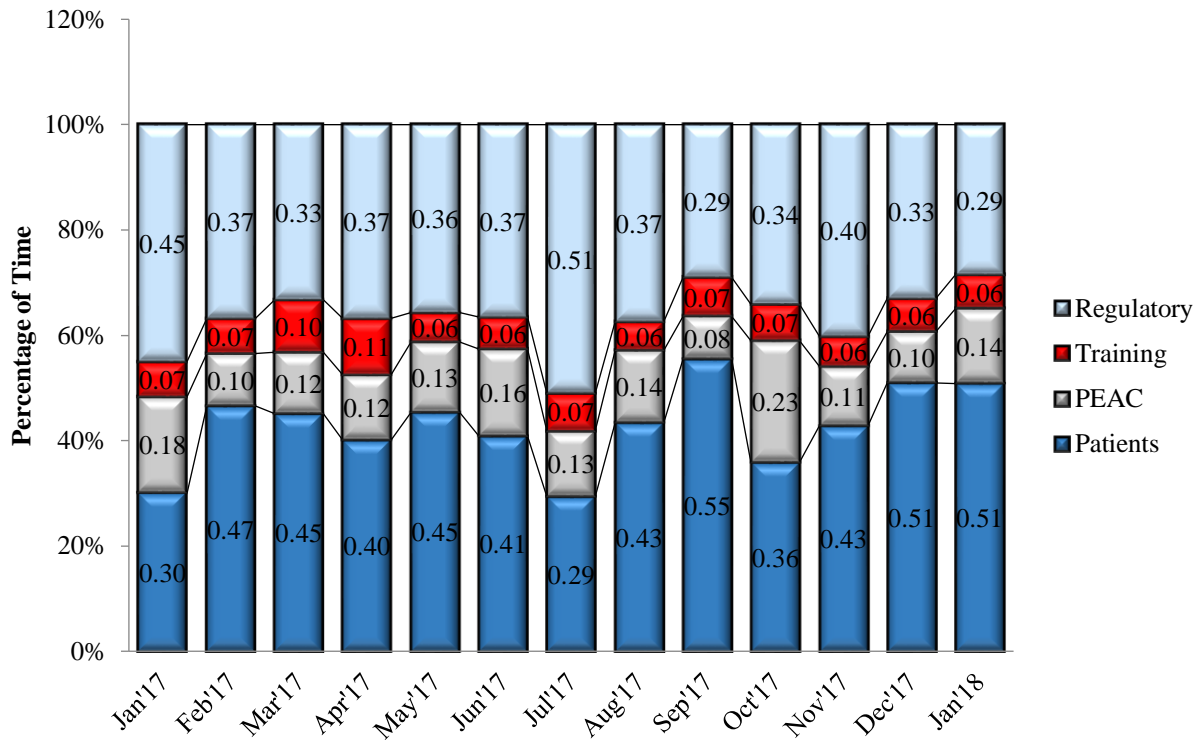
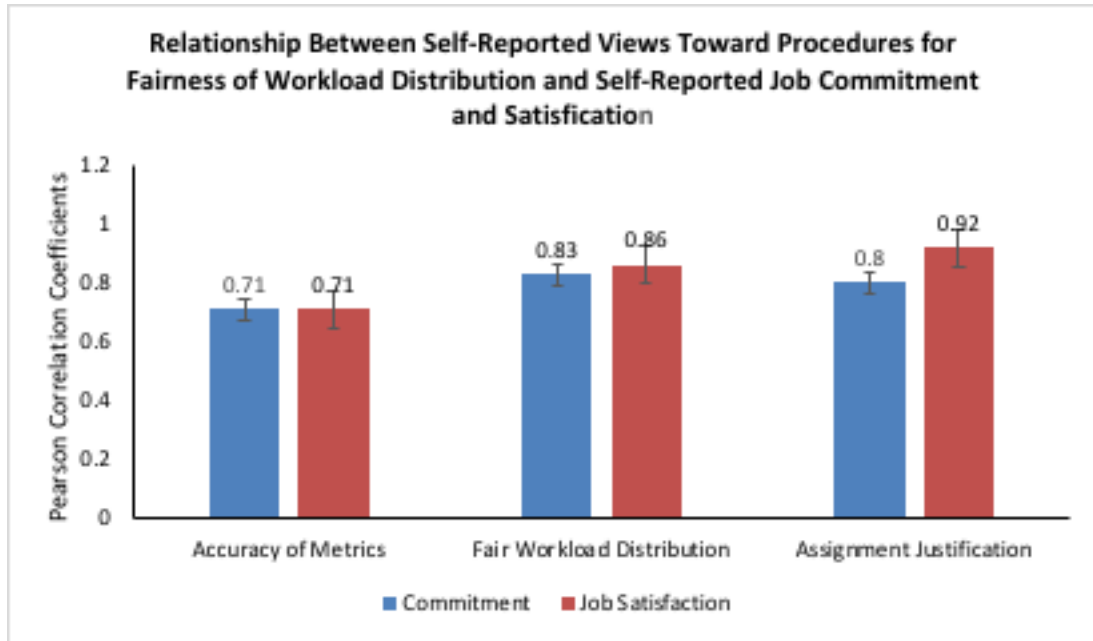


Figure 7: Mean percentage of time spent toward patient-facing activities was significantly increased from T1(M=.30, SE=.05) to T2(M=.51, SE=.08), $t(9) = -3.19, p < .01$, demonstrating increased efficiency over time as expected. Additionally, the increase in patient-facing activities coincided with a significant decrease in mean percentage of time spent toward regulatory from T1(M=.45, SE=.07) to T2(M=.29, SE=.07), $t(9) = 2.02, p < .05$.

Additionally, the retention rate of our coordinator staff increased from 40% (2016–17) to 86% (2017–18) post-implementation of the aforementioned productivity metrics system. Pearson correlations of the self-reported perceived fairness of the procedures for measuring and administering study workload assignments to the self-reported job commitment and satisfaction levels are presented in Figure 8.

Figure 8



Discussion

This paper focused on two adaptations of the OPAL productivity model considering protocol complexity, the number of procedures, and additional regulatory and administrative tasks to build a more comprehensive model and representation of coordinator workload.

Where the reproducible results of OPAL to improve efficiency and productivity in clinical research practice can be gathered from the data presented concerning two study sites, this paper elucidates how the benefits of efficiency are fostered through adapting certain metrics.

Specifically, these metrics capture the redistribution of workload across study roles to optimize and specialize staff, and more centrally, the value of encompassing additional workload factors for a more comprehensive and accurate model.

Moreover, a robust relationship between perceived procedural fairness of study assignments and workload distribution to self-reports of job commitment and satisfaction was presented, and is further bolstered by the 46% increase in retention following the introduction of adaptive

productivity metrics to a novel site (Children’s Health System of Texas). It is confirmed that understanding what additional workload factors the coordinators are managing and incorporating them in your adaptive metrics helps gain their buy-in and perception of fairness to improve their work-life balance, job commitment, and satisfaction to retain them as an asset to your program.

Additionally, the maturation of benefits that can be expected after several years using an adaptive productivity metric system (CRWT) includes increased funding support, as evident from the eight years of data presented from Stamford Health.

Conclusion

The model shown here offers great flexibility in both oncology and non-oncology settings, as it allows for continuity of care amongst study coordinators for their study participants. These metrics can be used to justify new and existing employees for research programs running clinical trials predominately on the high end of the acuity continuum. In addition, the metrics can be used to increase funding for additional coordinator and support staffing while improving study coordinator job satisfaction and retention at sites. This allows sites to achieve their enrollment goals and promote progress in their clinical research practice. In the wake of such improvements, research programs can expect more funding opportunities and greater success.

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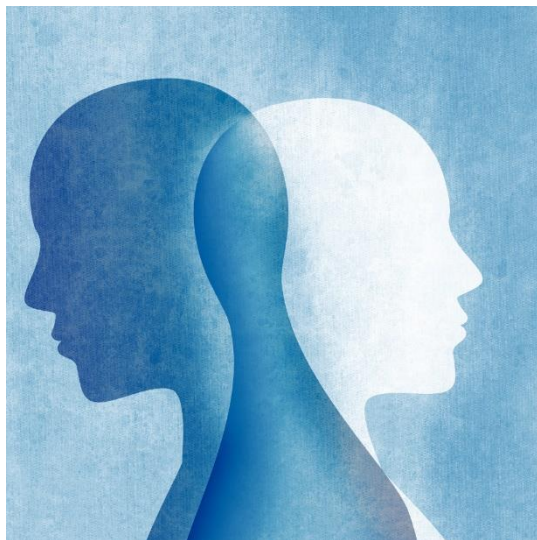
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SPECIAL FEATURE

Applying Behavior Change Strategies to Patient Engagement in Clinical Research

Mindy Gruba, MPH



Changing behavior—to some, it’s “second nature.” You just do it. As you grow up, you learn to pay your bills on time, you start calling your mom every Sunday, and you recognize the value of creating to-do lists. However, for some groups, or for more complex changes, the idea of changing behavior provides challenges each step of the way.

As a society, we sometimes attribute lack of follow-through to just forgetting. While that’s absolutely valid, people don’t just do or not do things because they forget, or because they remember. {1,2} In fact, people follow through on things because it’s easy (online shopping), there’s risk if they don’t (paying bills so they can continue to use their phone), their friends are doing it, or simply—they just enjoy it.

In the context of healthy behaviors, there are many tactics that health professionals employ to motivate their patients. These may include promoting tiny habits, such as “prescribing” a single, simple exercise, or explaining how medication can improve their symptoms. Patients may be especially driven when they start to experience the outcomes of being compliant, such as a reduction in disease symptoms.

With all that said, the ecosystem of what influences behaviors is highly complex, and can't always be attributed to a single thing. In the context of clinical research, taking a "health behavior" approach to help the person lends to this complexity. The intent of the trial isn't necessarily to make a person better, it's to answer questions. What makes this even more tricky is that patients in trials may not be getting better, either because they're in a control group or because there's no proof of effectiveness of the intervention.

How are Behavioral Tactics Currently Used?

With the rise in behavioral economics, we're now seeing industries begin to use and implement psychological insights to influence behavior through minute levels of persuasion, instead of coercion. {3} It's clear that this has improved desired outcomes for those who are implementing these tactics.

For example, there are some software services that default to a more expensive, yet unnecessary option upon checkout. The preselected offering isn't something you would have proactively chosen, but when it's the default, it feels like the standard. This may lead you to exhibit loss aversion. You now perceive your originally intended purchase as inferior, and a "downgrade" to be avoided. This revenue-generating tactic still provides choice, but nudges consumers to paying more than planned.

Conversely, we've also been seeing these tactics applied for good, such as default opt-in for organ donations and retirement saving plans, thus saving lives and building financial security.

Constructs of Behavioral Change Models

A behavioral change model relies on constructs to drive a framework that helps to understand the psychology of why people do the things they do. This can be used to drive strategies on how to influence those behaviors in a more desired direction, similar to the tactics previously described. {4}

While there are many behavioral models, most share the same or similar constructs. Table 1 lists a few of the key ones, and how to independently incorporate them into your patient engagement plan.

Table 1: Key Constructs of Behavior Change Models

Construct	What Patients Might be Thinking	Strategies
Perceived Risk	What is the likelihood something bad will happen? If something bad happens, how extreme will it be?	Inform patient of risks, focusing on susceptibility and severity of the condition or behavior (fear appeal) to convey importance of diligence, but emphasize methods for prevention and treatment to overcome risk to reinforce perceived efficacy.{5}
Knowledge	Do I understand what is being asked of me and why it's being asked?	Provide basic information about a medical condition that might include how the disease develops, its expected course, and how specific strategies can help manage it. Apply this same approach to study requirements, such as explaining why{6} patients need to take all their medication at the specified time.
Skills/ Ability	Can I stay organized and do I have the tools I need to be effective?	Provide patients with intuitive{3} take-home instructions and tools, such as easy-to-use pill boxes,{1} visit schedules, and preparation guides, along with reminders on their own phone. Help patients build good habits early in the study by anchoring to known habits that already exist. For example, if patients need to take a pill once a day, you could instruct them to take the pill just before brushing their teeth.

<p>Perceived Self-Efficacy</p>	<p>Am I confident in my ability to reduce the risk or attain the benefit?</p>	<p>Try the “foot-in-the-door” technique. First make a small, attainable request to build efficacy.{7} For example, have the patient complete a training diary at the site or review the technology with them so they will feel more confident about using it at home or on their own. Technology training is particularly valuable with older populations.{8}</p>
<p>Response-Efficacy</p>	<p>Will the outcome reduce the risk or increase the benefit?</p>	<p>Provide concrete examples of how risk could be averted.{5} In some trials, for example, a patient might be instructed to avoid certain medications. While it’s important to make them well aware of the risk, it should also be made clear that avoiding the drug can reduce the chance of a bad reaction. Giving specific examples, like brand names, makes it more concrete for the patient.</p>
<p>Subjective Norms</p>	<p>What are others doing? What do they think I should do?</p>	<p>Convey basic characteristics about others in the trial, such as how many are participating and what countries are involved, or show videos of former clinical trial participants describing their experience. Incorporate social incentives,{7} such as involving the caregiver in discussions to help provide additional encouragement and support throughout the study.</p>
<p>Attitudes</p>	<p>How do I feel about all that is required of me in the study?</p>	<p>Attitude may extend beyond self-efficacy, as it is shaped by beliefs and factors associated with a behavior.{5} For example, if a patient dislikes sitting in traffic and lives far away, he or she may be less likely to attend required visits. It can be valuable to measure attitudes at the</p>

		<p>beginning, and throughout the study, {5} via questionnaire, to determine how attitudes are shifting around the required study activities and to determine if intervention may be required.</p> <p>Explaining why patients need to do certain things can reduce perception of just being told what to do, decreasing resistance to change. {6}</p>
Motivation	<p>Do I have desire? Is it compelling, helpful, or interesting?</p>	<p>Get to know your patient to understand what drives them—intrinsically and extrinsically. {1,3} For those who are extrinsically motivated, praise them for completing compliance-based activities. You can also leverage reminder services to pre-program “why” and “affirmation” messages, so patients receive this reinforcement throughout the study. Help them feel a sense of accomplishment by showing progress in the study, or by conveying how their participation is helping research and may potentially help others like them, to motivate those who may be driven by altruism. This may be especially valuable when asking patients to participate in “extra” activities, like consenting to additional biopsies that aren’t required for trial participation.</p>
Intentions	<p>Am I committed to following through?</p>	<p>Intentions are largely driven by a combination of motivation, attitude, and subjective norms. {1}</p> <p>Work closely with patients to understand their intentions to follow through with study requirements. Use specific examples and outline a concrete plan of how they will achieve them.</p>

Triggers/ Cues	How will I remember to do these things, or when I need to do them?	Incorporate nudges that are anchored to a desired action, {3} such as sending reminders near or at the time patients need to complete a diary entry. As habits begin to form, patients may need fewer prompts, as constant reminders may create message fatigue. Shifting to targeted behavior-based notifications can help reduce this. For example, if patients are required to wear an activity monitor, only send targeted messages to those who are at risk of dropping below the required wear threshold.
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While addressing these elements independently has value, it’s sometimes helpful to incorporate them into an overarching strategy using the model to drive a more holistic strategy around engaging your patients. The model(s) you reference may vary based on needs{9}:

- Stage of the study (recruitment vs. in-trial)
- Protocol requirements (complexity and number of assessments)
- Study aims (prevention vs. treatment trials)
- Patient population (age, gender, indication)
- Region and associated culture (social constructs, motivations)
- Successful previous applications of the model in similar studies/populations

While there is an extensive list of behavioral models that could be leveraged, Table 2 presents a few worth considering. The sections following this table provide descriptions of the four models.

Table 2: Constructs Found in Behavioral Models to Consider for Patient Engagement

		Extended Parallel Process Model{4}	Theory of Planned Behavior{5}	Fogg Behavior Model{3}	The Information– Motivation– Behavioral Skills Model{1}
Constructs	Perceived Risk/Threat	✓			
	Knowledge				✓
	Skills/Ability			✓	✓
	Perceived Self- Efficacy/Behavioral Control	✓	✓		
	Response-Efficacy	✓			
	Subjective Norms		✓		
	Attitude		✓		
	Motivation			✓	✓
	Intention		✓		
	Triggers/Cues			✓	

Extended Parallel Process Model

The Extended Parallel Process model is intended to predict how people will respond to fear of a risk, given their level of perceived efficacy. Risk is inclusive of perceived susceptibility and severity, while efficacy includes self and outcome efficacy.

The model predicts that if people have high perceived risk and low efficacy, they will begin fear control behaviors by avoiding or denying the issue. Those with high perceived risk, but even

higher perceived efficacy, are motivated to begin danger control activities by taking action to reduce the risk.{4} This model is more often used to drive fear appeals by creating just enough fear to motivate someone to act.{10}

This may be applied to communication strategies for those with rare diseases or patients on their last line of treatment, who may tend to have lower risk perceptions to trial participation, given the alternative.{10} With that said, perceived outcome efficacy may be low in these populations, but potentially still higher than the perceived risk of the study, thus motivating them to participate.

Furthermore, within the trial, it can be valuable to heavily reward these patients for completing self-efficacy building activities, such as basic compliance requirements. In this context, patients in a Duchenne muscular dystrophy trial may experience learned helplessness, or a sense of powerlessness. It may be that physical therapy does not lead to progress for the patient, and no matter how hard the patient works, physical functions continue to decline.

When patients don't see a positive outcome from all their hard work, they may be more inclined to give up.{11} This is where focusing on compliance, such as rewarding patients by doing something within their control (e.g., wearing their activity sensor), can help to reinforce self-efficacy. It's also valuable to continue reminding them of how their participation is helping researchers find a treatment for others like them (outcome efficacy). This may motivate patients to stick with it, even if they're not feeling better.

Theory of Planned Behavior

This theory posits that a person's attitude, social perceptions, and self-efficacy can drive them to act.{5} A potential patient population to apply this model to would be children and adolescents, who are typically more susceptible to and impacted by social influences than other age groups.

Although children are required to consent to participate in a study, consent is also necessary from a caregiver. This could serve as an opportunity to emphasize to the patient that while he or she needs parental consent, the child also has a say in participation.

Targeting a child’s attitude toward the behaviors (visits, medication, tracking) may be more effective than just instructing them on what to do.^{6} With that said, education and assigning achievable tasks, with support from caregivers, can help build confidence early on in the trial.

As school-age children grow, they are increasingly more influenced by their peers and social environment.^{2} Leveraging social influences,^{7} such as describing basic characteristics about others in the trial (e.g., age and country), highlighting celebrities with the same or similar condition, or showcasing commercials or PSAs, helps reduce the stigma. This can help make trial participation feel more mainstream and “socially acceptable.” Caregivers can also serve as a source of social reward when young children feel like they are pleasing their parents by doing what is asked of them.

However, it’s important to use social strategies carefully. While positive reinforcement from a social network for high compliance can drive positive behaviors, it might prompt certain patients to feign compliance activities to please those in their social network. Therefore, one must find the right balance of rewarding compliance, while also rewarding honesty.

Fogg Behavior Model

The Fogg Behavior Model states that for people to be successful in performing a behavior, they need to be motivated, have the skills and ability to perform the behavior, and be prompted by a trigger. Strong presence of all three constructs equates to a higher likelihood of success. While a trigger must always be involved, motivation and skills do not both necessarily need to be high, so long as one of these constructs is compelling enough.^{3}

If someone is highly motivated, but has minimum skills to perform a task, motivation in itself might drive the person to acquire the necessary abilities. On the flip side, if something is easy, people might just do it.^{3} Take the case of store clerks who ask if you would like to donate your change or a certain small dollar amount to charity upon checkout. On your own, you may never have been motivated to donate, but in this instance, it is so easy that you agree when prompted.

Motivation can be quite elusive, given it is so unique to the individual. According to the Center for Information and Study of Clinical Research Participation, motivators for participating in trials are to help advance science and treatment of disease/condition, help others (altruism, or family), receive compensation, and to obtain better treatment. The top burden impacting ability is traveling to the study clinic. In fact, the top voluntary reason for leaving a study is the location of the study center.{12}

In clinical research, sponsors and vendors are working on various ways to remove friction and address the “time,” “money,” and “effort” abilities by presenting opportunities for patients to participate in studies more easily, whether by introducing remote visits, offering smartphone apps, or even providing childcare.

The Fogg Behavior Model may be applied to patients on two sides of the spectrum. For example, patients who are seeking last-line oncology treatment may be more motivated to participate, comply, and stick with a trial. Healthy participants, like in the case of certain vaccine trials, may not be highly motivated, but if it’s easy for them to do, they may be more likely to participate. This is especially the case if some extrinsic motivation can be addressed through compensation, including compensation associated with compliance activities.

In these scenarios, both groups need a prompt to participate, whether it be from a doctor for the highly motivated, or by passively being exposed to an online ad that makes it easy to sign up. Both groups would benefit from in-trial patient engagement strategies to trigger an action, like reminders anchored to the timing of an expected behavior (e.g., filling out a diary) and apps that prompt a call-to-action on a patient’s phone, which 90% say they “frequently” carry with them.{13}

The Information–Motivation–Behavioral Skills Model

This model suggests that factors that influence behavior include knowledge about the behavior, motivation to take action, and behavioral skills necessary to complete it. Not only must information and motivation be tied to skills, they must also link to the behavior change outcome.{1}

Information can motivate.^{2} An obesity study protocol may prescribe that patients complete specific health-behavior regimens, such as exercising and eating right. Patients need to be informed on what it means to eat right, and what type and level of exercise is most appropriate. They must also understand why and how this helps in the study. These guidelines, regardless of what arm of the study the patient is in, can reduce the patient's weight, therefore motivating them to comply.

Behavioral skills can be reinforced by providing tools such as pedometers or food scales,^{1} and “tiny habit” exercise reminders can be added into a patient's daily routine (taking the stairs instead of elevator, walking to a colleague's desk rather than messaging them, etc.).

Research has shown that patients immediately forget 40% to 80% of the medical information they receive, and about half of what is retained is incorrect.^{14} Therefore, these details must be made available to patients after their visits. Critical study information, presented in various formats, such as combinations of text, images, and interactive modules, can also be conveyed through the use of technology to target the diverse learning styles of patients.^{14}

Questionnaires can evaluate comprehension, and the results can be then used for targeted training to ensure knowledge is maintained.

Key Considerations

The common thread in these models is that many of the constructs can be leveraged to influence patients' way of thinking to promote specific behaviors. However, in some studies in which the endpoint is to measure changes in thinking, such as psychological symptoms of depression, initiating tactics to improve self-efficacy may be considered as interventional, and therefore needs to be navigated carefully.

Patients who are motivated by knowing they are helping to potentially take a drug to market may be inclined to report more positive results about how they are feeling, in hopes that it can help facilitate that process. While placebos can help offset this, it's important to reinforce to patients the value of answering honestly and to describe the benefits of being truthful when there are issues.

We also know that participation may be driven by motivation to potentially treat the disease. Again, it's critical to remind patients the intention of clinical research is to answer questions, and while the goal is to identify an intervention that is safe and effective, that is not the sole intention of the study.

Additionally, one must be careful in how fear appeals are leveraged to initiate behaviors. While it is important to emphasize to patients the importance and criticality of preventing and reporting adverse events, conveying such information must be objective and balanced relative to the risk. The key is to not overly and unduly communicate risk without emphasizing mitigation and escalation strategies.

To summarize, constructs and behavioral models are not prescriptive, but are intended to be referenced alone or in combination to help guide patients throughout the trial, and to help predict and reinforce or mitigate certain behaviors. So, whatever you opt for, approaching your patient engagement and retention strategies with a plan in mind can help improve the trial effectiveness and patient satisfaction. Why not give it a try?

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SPECIAL FEATURE

Getting Started with Using Social Media to Recruit Research Participants

Deaven A. Hough, MA; Elizabeth Flood-Grady, PhD, MS



Recruiting participants into research studies is one of the most difficult challenges we face as research professionals. The development of online tools, such as [ResearchMatch](#) and other participant-facing recruitment websites, {1} has enhanced research recruitment efforts. Study teams are also increasingly interested in using social media channels to bolster recruitment. {2}

At the University of Florida (UF), we’ve developed [guidelines for recruitment on social media](#) and launched a Facebook page, [UF Studies](#), as a central channel for recruitment advertising and general information about study participation. We’ll give you a glimpse of these initiatives here, and we plan to present on this topic live through ACRP in the near future.

Creating Guidelines for UF Research-Study Teams

Despite the expansive reach of social media, there are generally limited directives regarding their use for study recruitment. In 2016, our institution identified the need for a coordinated approach to address privacy, information security, and other questions pertaining to institutional review board (IRB) submissions to enable researchers to use social media in an ethical and compliant way to recruit research participants.

Social media have generated a great deal of enthusiasm as recruitment tools, but simply planning to “post on social media” isn’t enough to effectively and ethically recruit participants. To harness the power of social media for study recruitment, UF’s Clinical and Translational Science

Institute (CTSI) facilitated a committee and workgroup that endeavored to establish guidelines on *how teams and institutions can ethically and effectively use social media channels for recruitment*. Because multiple stakeholder groups are involved in the ethical recruitment of research participants and affected by social media recruitment decision-making, key stakeholders at the institution were involved in the development of guidelines from the beginning.

Dr. Elizabeth Flood-Grady presented a webinar featuring our process for identifying and engaging these stakeholders as part of the Trial Innovation Network (TIN) webinar series. You can [watch the webinar here](#) and [download the slides here](#) if desired.

Our guidelines emphasize:

- compliance with social media site terms of use;
- participant privacy, confidentiality, and data security; and
- procedures and considerations for using social media to recruit participants.

The guidelines focus on Facebook as the primary social media platform to recruit participants, due to the platform's expansive reach and large base of users. Facebook, the leading social networking site worldwide, offers billions of users the unique opportunity to access and exchange health information,{3,4} including information about recruitment and participation in health research studies. Other social media channels are reviewed on a case-by-case basis.

We invite you to [click here to read the full guidelines available on our website](#).

Facebook Advertising Through UF Studies

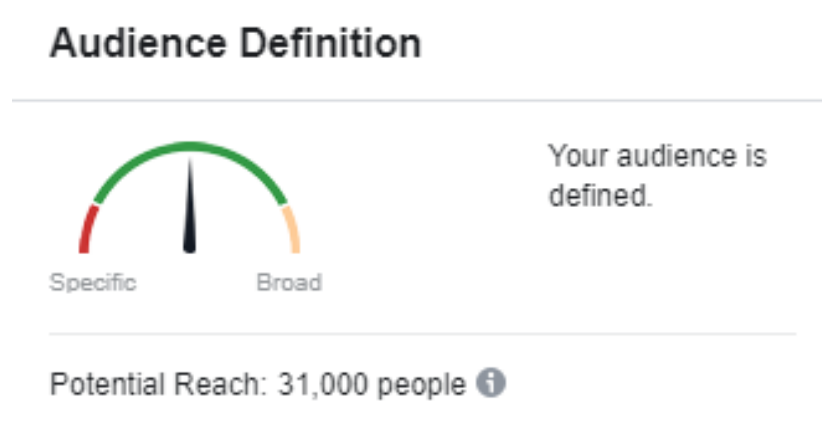
The UF CTSI's Recruitment Center is funded by a Clinical and Translational Science Award from the [National Center for Advancing Translational Sciences \(NCATS\)](#), and serves as a central resource for study teams interested in recruitment assistance. The UF guidelines incorporate the establishment of a central UF Studies Facebook page, which the CTSI Recruitment Center manages and uses to advertise studies at the request of UF researchers and to disseminate other relevant information about research and research participation.

The CTSI Recruitment Center provides no-cost consultations for research teams identifying and evaluating study recruitment methods, including Facebook, and creating comprehensive recruitment strategies for individual studies and grants. We conduct a feasibility assessment for teams interested in recruiting through Facebook paid advertising or Facebook groups and pages. The vast majority of our Facebook recruiting efforts use paid advertising campaigns. We create Facebook recruitment plans for IRB approval, launch IRB-approved plans, monitor campaign progress, and track metrics on recruitment. Here, we'll use a case study on recruiting adults for a Type 2 diabetes study to demonstrate this process.

Case Study: Diabetes

This randomized study's population is age 21–75 with Type 2 diabetes in the Gainesville, Fla. area. Exclusionary criteria include a diagnosis of Type 1 diabetes, drinking three or more alcoholic beverages a day, or diagnosis of Hepatitis B or C.

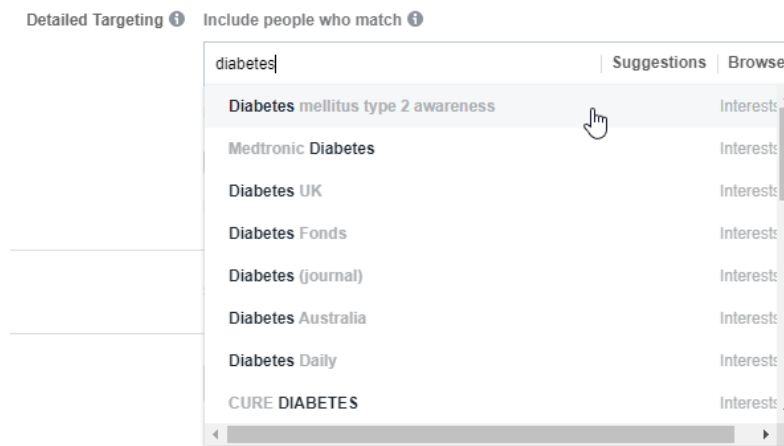
To see if Facebook would be a good fit for this study, we conduct a feasibility analysis in the ads manager function on Facebook. The ads manager is also where we eventually launch and monitor the campaigns. First, we select the target audience that we want to see the ads. Target audience is determined by selecting the targeting criteria, including location, age, gender, demographics, and any potential interests that are relevant to the population who will see study advertisements.



Click here to see [Facebook's infographic of all the areas teams can use to target participants](#). When we conduct a feasibility analysis, the goal is to have Facebook evaluate the audience as “defined,” and within the green section of the meter (as shown at left).

Study teams cannot target prospective participants by health conditions. Instead, they can identify and target prospective participants by health condition–related interests.

For example, we cannot target individuals with Type 2 diabetes, but we can target by interests related to the “Diabetes Daily” or “Diabetes mellitus type 2 awareness” (as depicted below). We recommend turning to the [Facebook Audience Insights tool](#) to identify additional interests for your target audience.



With general interests about diabetes, it is likely that individuals with Type 1 diabetes, an exclusion criterium for this study, may also see the ads. That is why developing targeted ad content, which is explained in detail below, is incredibly important.

The CTSI Recruitment Center creates a recruitment plan for the study team which contains:

- the list of targeting criteria (i.e., location, age, gender, demographics, and any potential interests);
- ad content, including a variety of post text, headlines, and images; and
- a description and link for where the ads will direct users.

The above considerations combine to make up a Facebook ad (see below).

The image shows a Facebook ad interface. At the top left is the 'UF Studies' logo. Below it, a box labeled 'Post text' points to the text: 'Adults diagnosed with Type 2 diabetes can play an important role in UF research. Compensation provided. Click the link below to visit the study website.' Below the text is a large image of a smiling woman with dark hair, labeled 'Image'. Below the image is the ad's headline area, which includes the text 'UFHEALTH.ORG', 'UF Type 2 diabetes study', and 'About two-thirds of people who are overweight, obese, or...'. A box labeled 'Ad link' points to a 'Learn More' button. A small information icon is visible in the top right corner of the ad area.

We create post text and headlines that are theoretically informed and based on previous successful Facebook advertising campaigns.

You can see in the ad we mention Type 2 diabetes in both the post text and the headline. Although adults with Type 1 diabetes may still see the ads, being as specific and targeted as possible in our ad content is an effective strategy for highlighting the relevance of the study to intended participants.

Images are selected from [Shutterstock](#), as every Facebook ad manager has no-cost access to Shutterstock images.

The ad link should lead potential participants to more information about the study. Our Type 2 diabetes ad shown above links to a webpage with more information about the study. This

webpage is what we refer to as a “study listing” that lives on our hospital’s website. The “study listing” is created by our CTSI Recruitment Center along with the Facebook plan with optimized content such as clear headlines and bulleted lists.

Linking the ads to study webpages with additional inclusion/exclusion criteria ensures the study team is not overwhelmed with requests from potential participants who would not qualify for study participation. In addition, by linking to a study listing on our hospital website, prospective participants see our health system logo and website URL and the study legitimacy is verified. {5,6}

Launching, Monitoring, and Tracking Campaigns

If the study team wishes to move forward with advertising its research on Facebook, we discuss the fees associated with using UF Studies and the CTSI Recruitment Center. Study teams are responsible for the cost of the campaign advertising and for CTSI Recruitment Center service fees associated with creating, launching, and monitoring the advertising campaign. The study team is also responsible for submitting all recruitment materials to the IRB for approval prior to launching a campaign on Facebook.

Once the study team has an IRB-approved plan, the CTSI Recruitment Center launches the advertising campaigns on the UF Studies Facebook page. Each campaign we launch on UF Studies allows us to learn more about recruiting participants using social platforms.

We won’t go into detail about the technicalities of launching the ads, but we do want to discuss monitoring Facebook ads. Let’s just say launching is the easy part.

Our guidelines address how to handle comments that reveal protected health information (PHI). For example, we had a Facebook user comment, “I am interested in the study, please call me at [phone number redacted]” and we hid the comment due to the reveal of the private information, even if it was self-disclosed.

The possibility of getting comments of this sort is very real, which is why having a plan in place to monitor, evaluate, and respond to comments is critical. Here at UF, we have a team that is available to help respond to or suggest deletion of comments.

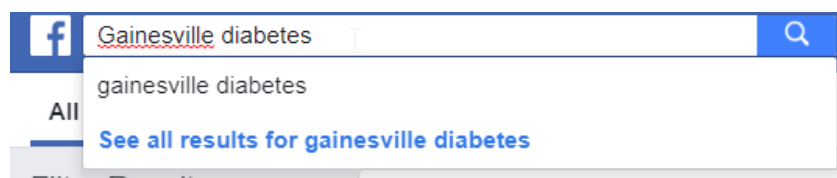
In addition to monitoring comments, we track campaign metrics through Facebook's ad manager function. This allows us to see how many clicks, people reached, and impressions the ad campaigns are receiving. We provide study teams with a weekly update on their campaign metrics and request data from them in return, including how many individuals contacted them because of the Facebook ads and how many participants they enrolled as a result.

Facebook Groups and Pages

Utilizing existing Facebook groups and pages is a good option for teams with a limited budget (it's free) and if there is a specific disease condition where pages and support groups exist.

Although posting in groups and pages is free, there is no guarantee that the Facebook algorithm will display the post to the intended audience. Paid advertising allows us to track metrics such as clicks, reach, impressions, and budget. Posting to groups and pages does not allow for those analytics unless specifically requested from the group or page moderator.

For our Type 2 diabetes study, we searched for groups and pages that are relevant to the study population in the local area.



When searching for groups, we want to make sure we are being as specific as possible. Posting to bigger groups might at first seem like a good way to reach large numbers of people, but can result in queries and questions that are difficult to manage due to the sheer volume of the audience you are reaching. Study teams must submit a social media management plan for these

posts to the IRB for approval; these plans must address not only how inquiries will be handled, but also how PHI posting will be addressed.

We do not recommend study teams join private groups. Instead, we suggest that the study team asks the Facebook page administrator to post on behalf of the study team. This not only protects the potential participants, but also relieves study teams from having to monitor comments and questions.

Results and Lessons Learned

So, does Facebook advertising work? We think so; since launching our UF Studies page in 2017, we have seen incredible growth in our page and paid advertising results (as of March 2020):

- 39 campaigns launched
- 39,000+ link clicks
- 868,000+ people reached
- 2,000,000+ impressions

Most importantly, nearly 1,800 participants have enrolled into studies at UF directly from paid UF Studies Facebook campaigns. Behavioral studies, particularly those requiring completion of an online survey, make up a large proportion of studies at UF. While some of our clinical trials are tough to recruit for and may not have any enrollments from Facebook, we still see a lot of engagement such as comments, likes, and shares from our ads.

As we move into 2020, we hope to understand a bit more about engagement on Facebook and just what sort of role it plays in recruitment. To date, our results demonstrate that Facebook advertising has incredible potential to enroll research participants, though a common concern is the ethics of this recruitment method.

When someone signs up for a social media platform, such as Facebook, they agree to the terms of use, but it is our responsibility to ensure that any use we make of the platform takes the rights and welfare of potential participants into full consideration. This is why we highly recommend institutions that are interested in using social media to recruit research participants take the time

to understand the roles and responsibilities of different institutional offices (e.g., the IRB will review social media content) and research teams (e.g., teams must adhere to existing social media policies enforced at the site). This also includes the permissible channels, strategies, and mandatory information to include in a social media management plan.

Perhaps one of the biggest lessons we have learned is that there isn't just one way to use social media—or even Facebook specifically—to recruit research participants. While other platforms have generated enthusiasm, we are continuing to evaluate our progress with Facebook groups, pages, and (of course) paid advertising. Having established relationships with your IRB, site communications team, and overall leadership is essential, as Dr. Flood-Grady describes in her [TIN webinar](#).

While Facebook shows promise, running paid ads or posting in groups and pages is not an automatic “win” for recruitment. When a study team comes to the UF CTSI Recruitment Center and expresses interest in using Facebook, we recommend a wide variety of services through our consultations and feasibility analysis. Indeed, we often suggest that study teams combine Facebook advertising with other services, such as ResearchMatch, our hospital's research registry, and our community engagement program, [HealthStreet](#).

The [UF CTSI](#) offers a wide variety of resources to study teams across the university, specifically research services like our [CTSI Recruitment Center](#). To strengthen our services, we work closely with the [STEM Center for Translational Communication](#) at the UF College of Journalism and Communications. Researchers and communications professionals from both groups work together to improve human health by incubating health communication research across disciplines and making scientific research more accessible, understandable, and usable.

As we continue to launch, monitor, and evaluate Facebook as a recruitment tool for research studies, we invite you to share your own social media recruitment experiences with us. We would love to collaborate with you and exchange information to ensure that study teams across the nation are using effective recruitment tools that are tailored to research participants.

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RECRUITMENT & RETENTION

How to Recruit, Cultivate, and Grow a Clinical Trial Subject

Danielle M. Desser, MS, CCRC, ACRP-PM; Courtney Dean Alexander, CCRC



Like learning to grow an exotic flower, subject recruitment, retention, and engagement is a delicate process in clinical research and full of potential stressors. Having a dependable principal investigator (PI) alongside a clinical research coordinator (CRC) can relieve these stressors. Especially in this current, unprecedented time in clinical research—with pandemic conditions prompting rapid adaptations for subject follow-ups while adhering to protocols and retaining subjects within the guidelines—finding ways to lessen site burdens is more important than ever.

Patient Recruitment

The saying goes: “You have one chance to make a good impression.” Is this true in clinical research? Scouring countless medical records in order to identify a patient who meets a protocol’s stringent criteria is the first step of clinical trial recruitment. Identifying patients who seem ideal for a study on paper is one factor, but there may be personal and environmental obstacles that preclude enrollment.

Certain patients are voluntarily engaged the first time the study is introduced. They may have been recruited by phone, heard about the study on the radio, or discovered it through research on the internet and then sought out the study site. However, given the medical benefits and risks, subjects also need time and family input in order to accept this important voluntary healthcare opportunity.

Further, the informed consent process requires an engaged PI and CRC working together, knowing the protocol thoroughly, and taking the time to answer any questions together to recruit a quality patient.

Retention

Once a patient has been successfully recruited into a research trial, the job is done...right? Not exactly. Clinical trials require, at times, lengthy duration of involvement on both the patient's and the site's side. However, how does one keep a patient engaged in a trial that requires daily diaries, paper drug accountability logs, and multiple visits to the site requiring extra effort on the patient than what they would generally incur?

The focus of retention is to keep patients engaged in wanting to participate in the needs of the trial, explaining the importance of the role they play, and capturing the much-needed data to move the trial forward. Retention requires a certain level of TLC, compassion, understanding, and going above and beyond the general call of the job.

Patients who are engaged and educated, and who understand the purpose of the trial, remain more engaged and responsive throughout the duration of said trial, and better at maintaining compliance for moving the trial forward.

Engagement

Even for trial participants who thoroughly understand the impact they are making on the future of medicine, researchers need to take a step back and remember these volunteers have responsibilities in their lives outside the realm of the study. Protocol deviations will occur, due to environmental and social factors beyond your subject's control, but documentation is vital.

Studies have adapted over to time to include motivational phone calls for helping keep subjects on track at completing their patient diaries, take their medications, or remember their next follow-up appointment. In long-term studies, it can be a challenge for study staff to remind subjects year after year that they have an investigational device or are taking an investigational drug requiring careful data-collection efforts.

Fortunately, sponsors have created patient cards and reminders for alerting participants about visits that might not be expected until a year later, but are nevertheless key to the ongoing study's progress. When the sponsor and study staff are actively engaged at set intervals, retention and engagement in clinical trials occur and could lead to a subject participating in a future trial.

Closing Thoughts

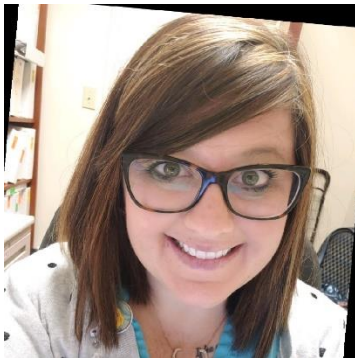
Patient recruitment, retention, and engagement are the driving forces for capturing the much-needed data for the clinical trials we conduct. Without recruiting ideal candidates who truly understand the need for them to be compliant, complete visits, and communicate routinely with site staff, the data captured are likely going to become unusable, incomplete, and costly to both the site and the sponsor. Retention of more subjects who don't become "lost to follow-up" is our ultimate goal, so going above and beyond to keep patients interested, on board, and up to date is paramount.

Engagement is probably one of the biggest issues sites face, because there is no single, standard tool that engages every single patient. Sites, in the past years, have had to become more creative and more involved in the engagement aspect—from offering perks while onsite, "swag" provided by trial sponsors, and routine follow-up not built into the budget between visits—so patients don't feel "lost" in the process.

In conclusion, efficient and effective recruitment, retention, and engagement by sites combine to form a significant contributing factor in the success of clinical trials, the award to sites of future trials by impressed sponsors, as well as patients who would enroll into more trials with the same site.



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SITE STRATEGIES

Fostering More Diverse Trials Through Targeted Protocols and Other Tactics

Jody Casey



In its recently released guidance, the U.S. Food and Drug Administration (FDA) has made clear its desire to encourage greater diversity in clinical trials.^{1} Diversity in clinical trials can mean more than just race; exclusions can apply to gender, age, sexual orientation, socioeconomic status, geographic location, and even social determinants of health.

Further, a recent article from *Outsourcing-Pharma.com* highlights a phenomenon of overrepresentation of white males in certain cancer studies, which is happening across academic institutions in the U.S.^{2} The article states why this is so problematic: Treatments designed with such a narrow sample will not reach a diverse population.

Different populations and age groups respond differently to medications and treatments. This is something that the medical community knows, but that sites may not identify or prepare for within traditional research protocols, which often results in a homogeneous patient base (most typically white males).

Recognizing and Addressing the Barriers

Despite general agreement that diversity brings key benefits to both patients and to the quality of evidence generated, overcoming barriers to including a more diverse population in clinical trials has proven to be challenging.

One critical way for sponsors and contract research organizations to address the lack of diversity in trials is to run protocols within healthcare practices that largely serve minority communities. By bringing clinical care directly to patients in their own communities, trials are more likely to reach a diverse population, including participants who would otherwise be excluded from the research process. This approach enables easier patient access to trials while maintaining the trusted relationship between the patient and the physician.

In Texas border cities like El Paso and Laredo, patients are often unsure of research opportunities outside their current physicians' practices, and are less likely to seek them out—or to even be aware they exist. Among large populations of immigrants and first-generation Mexican Americans, there is a very real comfort and security associated with their trusted physicians. Having their medical history already on file is important to them, and helps with engagement.

Another reason these remote areas are also largely underrepresented in trials is because patients often don't have access to reliable transportation, making travel to large academic medical centers, often located hundreds of miles away, inconvenient and cost-prohibitive. This is one of the key barriers to accessing trials.

In addition, there are barriers to entry for local doctors who wish to conduct research. Border communities are generally designated as “underserved,” meaning there's a worse-than-average doctor-to-patient ratio.

Yet another challenge is the economic impact on patients. Many patients in the working class do not have the extra time required to participate in a study and aren't allocated time off.

What's more, the high demand for physicians means most practices don't have the time, resources, and staff to start up trials on their own. With the burden of time commitments and start-up costs, the pool of healthcare experts and patients currently able to participate in clinical research is not ideal.

Conclusion

By tackling all of these barriers, from both the patient and the physician side, institutions and organizations involved in clinical trials can better pursue their missions of enabling greater access for more patients. Providing healthcare practices with the technology, staff, resources, and infrastructure needed to participate in trials will help to advance better treatments, for more patients, well into the future.

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SCIENCE & SOCIETY

Decentralized Clinical Trials: A Much-Needed Plan for a More Reliable Future

Al O. Pacino



A new foundation is being set for clinical research where connectivity and responsiveness are prioritized. Patients and clinical research staff can experience fewer obstacles and more time participating in therapeutic breakthroughs by maximizing the use of global data privacy and security tools. Rapid innovation has brought us to this moment, and it's time to embrace the future of clinical trials.

Clinical research professionals working at all levels for sites, sponsors, and vendors are currently facing significant challenges related to COVID-19. Hospitals and other health-related organizations are feeling the pressure of overcrowding. Clinical trial sites are still expected to maintain regulatory compliance while also delivering efficient care. Governments are rapidly adopting or developing plans of action that require businesses that handle personal information to have individuals “own” their data.

Businesses and hospitals are also expected to comply with “social distancing” efforts while providing the necessary tools to care for patients. With the demand for vaccine development and need for healthcare workers’ attention at an all-time high, we need to look at all options. It is time to seriously consider decentralized clinical trials and telemedicine as modern-day solutions to addressing not only the existing pandemic, but as tools and tactics to be integrated as ongoing, reliable tools in the clinical research industry.

Telemedicine: Improving Participation, Increasing Care

Several health insurance plans now offer telemedicine as an added service among their coverage. Companies such as Lyft are providing transportation services to those who need to commute to their clinical appointments via their mobile app. Decentralized clinical trials are getting a second look based on the COVID-19 impact and the overall direction of the high-speed, tech-driven economy.

The demand for these types of services have only increased due to a variety of factors. Requiring many staff and patients to be at home in isolation means many new needs are arising to be met with innovation. It is becoming essential to keep clinical research robust by creating space for global service providers to “meet” all in one place for the benefit of every professional tied to this vast enterprise.

An industrywide goal ought to be the development of specific guidelines and standards for the success of decentralized (or virtual) clinical trials. Consequently, establishing direct lines of communication between patient and staff can also increase the success and popularity of telehealth methods. Normalizing the electronic exchange of patient records and data seems to be inevitable, especially when there is strong enforcement of lockdown ordinances during moments of crisis.

Decentralized clinical trials are providing the infrastructure necessary to adapt to the needs of patients and clinical research staff. An added benefit of decentralization is that it addresses the need of decreasing data variance. Patient populations, many of whom are currently quarantined in their own homes, are in a moment where help is often needed and the potential to provide care is abundant. Existing technology, when combined with strategic marketing, can allow researchers to grow the diversity of their pool of patients and as a result help with the data variance issue.

General Data Protection Regulations: Protecting Health, Security, and Competencies

Currently, too many barriers exist in the early stages of clinical trials for decentralized trials to achieve time-sensitive outcomes. Standardization of telebusiness guidelines can help lower the time it takes to get a product to market.

The ability to assess proposed telehealth solutions based on industry-generated guidelines could pre-empt and decrease the bureaucratic requirements of regulators such as the U.S. Food and Drug Administration. Standards can fold in the regulatory expectations of the General Data Protection Regulation (GDPR), which compels organizations handling personal data to be accountable to users submitting their information. Most businesses are managing their clients' information via decentralized platforms. It would be to the benefit of clinical research organizations around the globe to keep in mind the stringent demands of GDPR and to have the necessary data protection staff and protocols in place.

A step that can be taken is to create an online mechanism where decentralized trials and telemedicine companies are able to professionally align compliance requirements, while finding common ground for tackling areas of focus for research. Streamlining existing electronic siloed systems is going to save many professionals time, money, and resources that are becoming more precious by the day. Efficiently handling the modern demands of data safety and limiting data variance in our current environment is essential for creating site sustainability.

Conclusion

Technology that allows for the sharing of data across the healthcare and clinical research ecosystem has often been met with heavy amounts of skepticism. As a society, we experience innovation in other areas of our lives. By establishing standards, we can begin to embrace more of these solutions and to deliver to patients and survivors the sense of ease and simplicity they deserve when it comes to receiving care.

The clinical research industry is on the frontlines of leading all of us to a new world where—regardless of location, race, gender, or socioeconomic status—a relationship between clinical research staff and patients can be made. However, it is becoming an imperative to limit the number of in-person attendance at sites for the sake of a clinical trial. We must protect as many vulnerable populations as much as possible, particularly in light of COVID-19.

Now more than ever, it feels vitally important to be part of the solution in the fight to save lives.



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ETHICS IN ACTION

Research During an Epidemic: How Can We be Prepared?

Lindsay McNair, MD, MPH, MSB



As I write this column, COVID-19, the illness caused by the SARS-CoV-2 virus, is wreaking havoc on societies and healthcare systems across the globe. COVID-19, which was officially declared a pandemic by the World Health Organization (WHO) on March 11, 2020, is an infection that attacks the lungs, causing significant damage from both the infection and the resulting immune response. Any numbers will be completely out of date at the time this column is published, so I will say only that the United States

and the majority of countries affected are still on the uphill side of the incidence peak, with various forms of social engineering being used to try to “flatten the curve” and reduce or spread out the total number of cases so that healthcare systems are not overwhelmed.

Of course, the very reasonable questions being asked in this situation are about what else we can do. Is there a vaccine that can reduce the size of the population at risk? Are there therapies that can minimize the chance of significant disease once infected, or that can support those who have severe lung complications to increase the survival rate? (Actually, we know there are not, because how could we have developed ways to treat a virus that we’d never encountered before?)

We've Been (Close to) Here Before

Which brings us to our current position of doing research in the midst of a pandemic. It's not the first time that the international research community has encountered this kind of situation.

In September 2014, an Ebola outbreak in West Africa brought this issue to everyone's attention. The world prepared for the possible spread of the infection, and the research community directed resources toward potentially effective therapies. However, with no research infrastructure ready to come into place quickly, and difficult ethical questions being continually debated, it was six months before one of the most promising agents was first dosed in a clinical trial in March 2015. That seems like a fairly speedy start up process for most clinical trials, but in an epidemic, it is an eternity.

The Ebola trial was able to dose only 72 participants between March and November 2015, and closed enrollment in January 2016, far below the intended sample size of 200 participants, due to the decreased incidence of new cases in West Africa. While the end of the outbreak was good news, it also meant that the question of the efficacy of the study drug could not be definitely answered from the resulting underpowered study, leaving us unprepared for the next outbreak.

Where to Now?

So how can we prepare in advance for research in epidemic settings, in a way that will let us prioritize experimental agents, launch trials quickly, collect data cleanly, and get rigorous answers? The following are some of the things that the international clinical research community can think about, and ideally decide, in order to prepare.

First, and most basically, we can create the skeleton of a clinical trial design that allows rapid adaptation to the specifics of the clinical characteristics of the epidemic, and a quick launch into place once potentially promising agents are identified. Platform studies, which allow the assessment of multiple potential agents, either in parallel or sequentially (first with one agent, then when that one reaches an efficacy or futility determination, moving on to the next agent in the same trial), may be ideally suited for this.

In the COVID-19 outbreak, the WHO has already announced the initiation of a platform study called SOLIDARITY, designed to assess four different study drug regimens.^{1} The study, which does not have a control arm, will accept online registration of potential participants by the treating physician, with consent e-mailed to the site and returned electronically. Randomization assignment will then be given based on which of the agents are already available at the local institution.

The SOLIDARITY trial is designed to minimize burden on caregivers with regard to administration and data collection, given the stress they are under to provide clinical care. This is a significant consideration; in these settings, the investigators may very likely be research-naïve, and trial sponsors will have to think about which data are absolutely essential to collect rather than interesting to have.

Thinking Things Through

Second, the global clinical research community and research ethics community can also discuss and try to come to consensus on some of the ethical questions and priorities—or to at least narrow the discussions so there are fewer real-time decisions to be made. For example, should clinical trials in epidemics include a standard therapy control group if we know the response to standard therapy is poor, or should everyone enrolled get an experimental agent? Giving everyone access to (unproven) study drugs feels more like “doing something,” but it could also mean doing something even more harmful than nothing.

Along those lines, what should be the role of expanded access/named patient/compassionate use programs, which provide experimental therapies in a way that collects little or no data to be able to assess outcomes? Should there be a minimum level of data that indicates a favorable balance of efficacy and safety before making a product widely available? This question becomes even more important when the therapy is already marketed for a different purpose, and the only thing limiting its use is the behavior of prescribers.

We are seeing this in the COVID-19 setting, where a very small, poorly controlled, self-published study touting the antiviral effects of a certain medication has set off worldwide

prescribing and even hoarding of the medication, with the well-designed clinical trials barely begun. If preexisting “miracle” drugs can be accessed anyway and patients, families, and the media are convinced that they will work, it may be very difficult to conduct controlled trials on any of them now.

Who should get first priority for clinical trial enrollment—healthcare providers who are most at risk? Should children be enrolled in early studies, or should enrollment of children wait until data are collected in adults?

In any epidemic setting, the specific characteristics of the epidemiology and clinical picture will certainly impact decisions. For example, since COVID-19 seems to largely (although not completely) spare the very young, considerations about enrolling children are not being widely debated, although they might in a different epidemic where young people were more at risk.

Similarly, the design of the intervention and intended use will also guide some of these questions; in a study of post-exposure prophylaxis, healthcare workers who are being frequently exposed to the pathogen may be the best population in which to conduct the study most efficiently. Control arms may be considered widely acceptable if the study only includes patients with mild disease.

So, we can't answer every question in advance, but we can list the questions that we will need to think about and form a group that can be prepared to come together and resolve them on short notice.

The Risk of Losing Focus

Third, perhaps the biggest challenge to planning for research in a future epidemic may be driving both interest and resources to prepare for a crisis that has not yet, and perhaps may never, actually happen. Dr. Peter Hotez started working on a vaccine against coronaviruses in 2003, after the initial SARS outbreak, and he and his team had a candidate ready to go into human trials in 2016.^{2}

However, with no apparent risk from coronavirus at the time, Hotez was unable to get funding to move his project forward and clinical trials were never started. Flash forward to today, and it will take months for his team to get back to where they were when the project was put on hold. Similarly, discussions of potential trial designs and ethical quandaries will need a strong and impartial body to organize and drive discussions forward, when it can always seem like immediate issues need to take precedence over hypothetical future ones.

Hopefully, as some of the lessons from the Ebola outbreak provided us with information to help us better prepare for COVID-19, some of the lessons we learn from COVID-19 will also help us plan for the future.

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5 Lessons Learned from Clinical Trials While Facing a PANdemic

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As the world faces the novel coronavirus causing COVID-19, a quick trip to the grocery store provides a glimpse of some of the panic growing in communities. Work in clinical trials has provided lessons in focus vs. fright. I share these lessons to help promote focus and dampen panic:

- **What's the data source?**

As I write this in March 2020, information on COVID-19 is EVERYWHERE: some wild speculation, some expert opinions, some facts... Just as you would before documenting data on an electronic case report form, *consider the source*. Is this information from a reliable source (e.g., the Centers for Disease Control and Prevention) or is it based on a viral Facebook post? Consider the source before further documentation.

- **Diagnosis isn't everything...**

Eligibility for treatment under a clinical trial is dictated by the defined protocol inclusion and exclusion criteria. If a patient has a disease, it does not necessarily mean that they qualify for treatment. With the wide range of reported symptoms associated with COVID-19 to date,^{1} diagnosis is only part of the treatment algorithm. *More information is needed.*

- **Keep objectives in mind and amend the plan as necessary**

The protocol details *how* the clinical trial is to be implemented, sometimes exceeding 100 pages in length. The study objectives section of the protocol clarifies *why* the trial is being completed. Protocol amendments alter the plan (protocol), while remaining focused on the study objectives. With social distancing measures, school closings, and an increase in telework, implementation plans may require re-evaluation; focusing on *meeting the overall objectives*.

- **Timely and effective communication**

Many study communications have defined due dates, action items, and resolutions (think institutional review board/U.S. Food and Drug Administration submissions, monitoring

follow-up letters, etc.). This structured communication sets expectations and forms a closed loop of effective communication. While many are now working remotely or in very different working conditions, *please don't assume* everything is status quo. Ask, receive a response, and ensure team members are on the same page.

- **Risk review**

In accordance with Good Clinical Practice guidelines, sponsors periodically review risk control measures for effectiveness and relevance, based on emerging knowledge. {2}

Thanks to the dedicated efforts of those on the front lines of this virus, available information is continuously updated. Continue to follow reliable sources for *updates in risk control measures*.

Please follow the guidance of your public health officials. Thank you to all our first line responders and hospital staff who continue to serve the community. Please stay safe. We will take this one day at a time.

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