APRIL 2014

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# *A Theory on* ***Site Engagement:*** Why Early, Dynamic Interaction with Clinical Trial Investigators Avoids Problems and Saves Money

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[DOI: 10.14524/CR-13-00057R1.1]

Study site staff want unencumbered access to the sponsor team, and talented trial leaders are naturally inclined to connect with the people involved in their studies, establishing relationships quickly within and across the entire community, no matter how large it may be. These leaders do more than listen and respond; they recognize that effective site support is inexorably linked to the depth of what can be learned about how people actually carry out their responsibilities. Then they face those realities head on.

## SPONSOR STORY

Years ago, I resolved to bridge the gap between our study teams and site personnel—a gap that inevitably appears when we partner with contract research organizations to help run our studies. My signature initiative to address this problem was to find ways to engage personally with the nurse who consents our patients or the coordinator who records our data.

Last spring, while preparing a conference workshop on this topic, I was stunned to realize it had been more than a year since I had spoken with anyone at a study site! I shared this sorry fact with the workshop participants, and wondered out loud if I could demonstrate sufficient relevance not to waste their precious time. A hand from the audience shot up. "Call us," the attendee said. "It doesn't matter. We want to hear from you."

I can tell you, that feedback was some motivation for me. I did my homework and made my first call to one of our investigators later that day. I learned something new, agreed to find an answer to a question about a prior study, and called the investigator back the next day with new information. This pattern repeated and, within a few days, I had spoken with seven of our sites, deriving a rich body of feedback that changed my perspective and influenced decisions.

My team members who model this behavior insist it calms what might otherwise be tense problem-solving scenarios and increases responsiveness to enrollment campaigns. However, I am bothered by this persistent question: How can return on investment of sponsor-site contact be measured? It certainly cannot be done justice with a mathematical equation.

One thing I can say with certainty is that my direct and unfiltered interaction with the people who work on our studies is imperative to my ability to do my job.

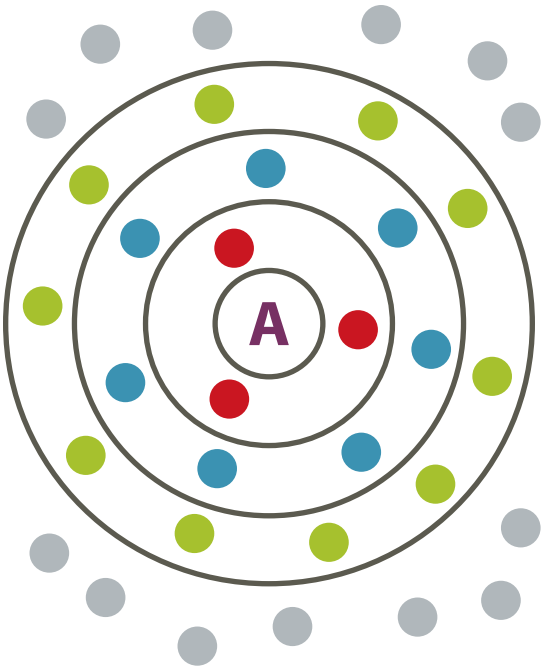
*— Eileen M. Daniel, Senior Director, Development Operations, Endo Pharmaceuticals*

The clinical research conference circuit has been abuzz with two topics in the past year: risk-based monitoring and site engagement. Although the former is objective and rooted in comfortable parameters, like visit counts and source verification percentages, the latter is an emotion-based, philosophical discussion. Sure, we can quantify the outcomes of site engagement in terms of improved enrollment rates, query resolution times, and the like, but these metric-based performance assessments skip over what it means to cultivate relationships between disparate members of the clinical research enterprise.

Generally, people involved with clinical research are scientifically curious, process-oriented, and driven by the pursuit of data; however, subconsciously they seek to understand their colleagues' motivations and ambitions. This natural behavior results in so many of the person-to-person interactions throughout the workday that are fundamental to human experience, there is little recognition of a need to discuss it.

The problem is these interactions do not extend so naturally across all the people, boundaries, and distances in the larger clinical study context. When the community does not promote, or worse, obstructs natural person-to-person interaction, bad things happen.

**FIGURE 1.** Coworking

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## Engagement Theory

People engage with one another around an ambition or motivation. A person can be directed to talk to a counterpart, but he or she cannot be forced to engage in meaningful discussion. That comes only from mutual interest in a topic or each other.

Identifying a common motive for a study coordinator, regional monitor, principal investigator, and pharmacist in a clinical trial can be a daunting task. Consider a simple example: Ask yourself why you are reading this article. The authors hope you find it interesting and worthy of your time to read it through to the end. To be transparent, we also admit the value of exposure this publication offers and know it will have some effect on our reputations in the industry.

On the other hand, what might be the motives of ACRP for publishing this article? Without a doubt, the association wants its readership to acquire some new insights, but it also needs *Clinical Researcher* to be valued enough that memberships (and therefore, access to the publication) are renewed.

Buried in this example is a common goal of learning that could be easily diverted by the ancillary goals of any of us—reader, author, or publisher. In thinking about strategies to engage people in a study community, those ideas must be evaluated through the lens of each stakeholder.

Once a truly common motive is identified, a platform emerges for engaging members of the community. Creating small experiences in which people may share their participation is the first order of business.

Figure 1 is a model on building communities as part of the "coworking" movement, portraying a vibrant community comprising members with differing degrees of engagement. Their level of involvement spikes and drops off over time, with every person traveling along his or her own continuum.

As people mobilize around a motive or ambition (A in the figure), they all start as Observers. An Observer receives information, but is not expected to do anything further. Over time, given additional opportunities to participate, some members of the community will step out of the crowd to join in the discussion. We call these people Attendees: They respond when a question is raised and are present when an event is scheduled. Creating opportunities for one or more Observers to become Attendees is the first objective of building a community.

After some time has passed, with the right occasions available, a number of Attendees may contribute without prompting. These contributions might be suggesting improvements, raising new questions, responding to others, even critiquing. The people in this new subgroup are called Participants. They are the first sign a vibrant community is developing and on the way to self-sustaining.

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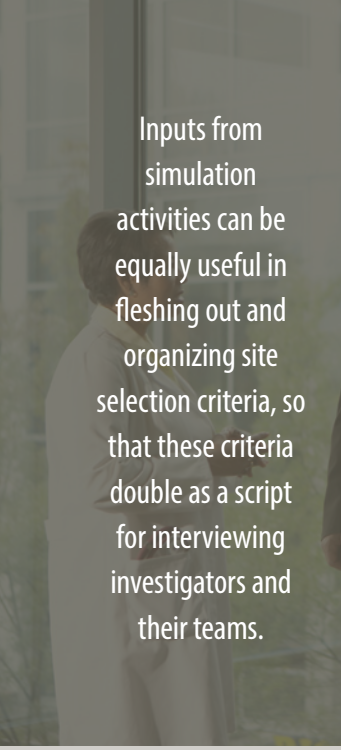


Inputs from simulation activities can be equally useful in fleshing out and organizing site selection criteria, so that these criteria double as a script for interviewing investigators and their teams.

Eventually, one or two of the membership might become "super"-participants. These are highly engaged individuals who identify so strongly with a motive that they engage at all levels with the community at large and gain the respect and trust of everyone. We call these people Champions.

## Danger, Danger

This is not a race to the center; nobody is obliged to move through all levels of participation or become a Champion. Some members will become more involved; others will not. Deeper levels of involvement by some may be sustained, or may drop with shifting priorities. This is all okay.

A community manager must recognize when and where participation levels need a boost and create an occasion or inject something newsworthy to keep the momentum going. Further, he or she should intervene when a person or subgroup becomes over-involved, as other members may feel alienation, burnout, or possibly distrust as a result.

Applying this model of engagement theory to the clinical trial arena requires early creative thinking on the part of the sponsor team, as it expands beyond its core members—ideally after the study concept is stable and before the protocol is final. The case examples presented next are timed prior to study start, well before investigator sites receive regulatory paperwork that signals commencement of site activation. They represent some of the most consistently missed opportunities to begin building a community of interest around the clinical program and reaping the benefits of engaged membership.

## Case 1: Protocol and Site Feasibility

The site feasibility process is one of the first levers pulled when the clinical trial machine kicks into gear. It spits out hundreds of questionnaires aimed at determining how many patients a site may have, where its centrifuge is, whether it has a pharmacy, how many other studies it may be running in competition, and so on. Responses are sorted; triage meetings take place; and teams are deployed to follow up by e-mail, phone, and fax.

Sites that make the cut receive the paperwork and the pre-study site visits (more on that later). Frequently, feasibility stops there, leaving the illusion that the institution (the site) is known to the sponsor and that a mountain of paperwork already exists to prove it. However, it is all too likely that we have learned little about the people at the site and we have missed an opportunity to influence how they will behave once the study gets started.

Described next are tactics that Endo Pharmaceuticals followed to create an early participation experience that served to establish and deepen relationships. The feedback obtained was used to inform and improve the operational execution of the protocol. Any sponsor or contract research organization can do the same thing.

### Involve and Engage Candidate Sites Pre-Study

Referring back to engagement theory, the large pool of candidate sites receiving a feasibility questionnaire would be the Observers. In this example, a subset of investigators was selected to participate in a private online discussion based on their expertise in the therapeutic area and for their passion for patients. Prior to the internal deadline for final protocol, a draft was posted in an invitation-only, secured community that included a discussion forum where specific questions were posed. The trial leader sent a personal e-mail to each investigator with an invitation to join the protocol review team and instructions for accessing the protocol online. A follow-up phone call was made to underscore the importance being attributed to their feedback.

### Let Sites Talk to the Study Team and Each Other at Will

Busy investigators reviewed a PDF of the draft protocol from their home or office computer, tablet, or phone. They were asked to answer six questions in the discussion forum, either via the website or simply by responding to e-mails (relayed through the forum to keep everyone updated) on topics of endpoint analysis, lab values, and relevant concomitant medications. The first investigator to respond had the most to say, arguably making it easier for others to weigh in with agreement or counterpoints. Study team members interjected with answers to investigators' questions; then, instead of waiting for the next protocol draft to see others' comments, they could respond right away.

### Outcomes

There was one significant, and measurable, outcome: Investigator participation in the protocol review team resulted in the elimination of a secondary endpoint that would not have been feasible to collect; hence, a protocol amendment was avoided. An equally significant outcome, albeit a less quantifiable one, was that a broad segment of the sponsor team was exposed directly to investigator feedback. The forum discussion provided valuable context, and was used as-is to inform final protocol revisions. A commitment was made to evaluate each suggestion and to provide investigators with the rationale for changes that were made.

As sites were activated, new Observers and Attendees (coordinators and investigators) became Participants as they used the forum to pose questions. Study team members replied online and called to ensure all their questions were answered satisfactorily. There was no need to create a process to manage frequently asked questions in a spreadsheet.

## Case 2: Pre-Study Site Visit

How would monitors and site staff describe what is expected of them during a pre-study site visit (PSSV), and what is the deliverable? An appropriate answer would be that the deliverable is a monitoring visit report, complete with ticks in all the right boxes and ready for regulatory inspectors.

## SPONSOR STORY

Simulation is another tactic that can enrich the feasibility stage by turning it into an opportunity for early engagement; we do "deep dives" on protocol eligibility criteria by simulating how a site might identify those potentially eligible and acting out the patient experience before the protocol is final. We use the inputs from these exercises to create interactive investigator meeting "how-to" sessions.

Dave Munneke of American Medical Systems says research coordinators are great partners in walking through the protocol from both site and patient perspectives, and they are instrumental in developing case studies for the investigator meeting, now called the study initiation meeting: "We identify learning objectives at the outset and anonymize patient files for coordinators to simulate data collection. We then facilitate dialogue in parallel groups of five to seven participants. The goal is for [meeting] participants to encounter learning opportunities and walk away from the meeting well equipped to conduct the study. This format also allows us to tap into the collective experience of all participants."

Inputs from simulation activities can be equally useful in fleshing out and organizing site selection criteria, so that these criteria double as a script for interviewing investigators and their teams. Such interviews, when done by study team leaders skilled in transforming the question-and-answer routine into actual conversations, are a valuable first opportunity for people to forge relationships based on things they mutually care about. When that magic happens early, bonds are created that survive and thrive through the inevitable peaks and troughs of a clinical study.

People are more comfortable talking about uncomfortable topics when there is a respected and valuable relationship in place. Operational difficulties in clinical trials are largely overcome due to people's willingness to discuss things that aren't working well.

*—Kathy Goin, Vice President Clinical Operations, Trevena Inc.*

However, what if the deliverable included engagement? To put a sharper edge on a seemingly soft objective, make the PSSV a forum to uncover exactly what principal investigator oversight will mean for the site.

"Sample procedures and forms don't show that," according to Leigh Kerr who directs and oversees clinical studies at Endo. "You can't see actual documents that demonstrate oversight during feasibility or during the PSSV. More and more, we have to go to sites we have not used before, and sponsors simply don't share data on past performance [with other sponsors]."

Even with near-perfect execution of study steps, the danger of protocol violations is still high if investigators and their teams do not get an opportunity to engage in dialogue that increases their understanding and addresses sponsor concerns.

"Protocols these days are operationally difficult to envision," Leigh continues. "We engage to identify where a trouble spot may surface."

Supplementing the prescriptive PSSV with a candid conversation during which mutual expectations can be put on the table instills confidence with the investigator and his/her staff, as well as with the study team. The prerequisite step to making a PSSV this valuable is to do one's homework and get the study team to align on what it needs to get out of the visit.

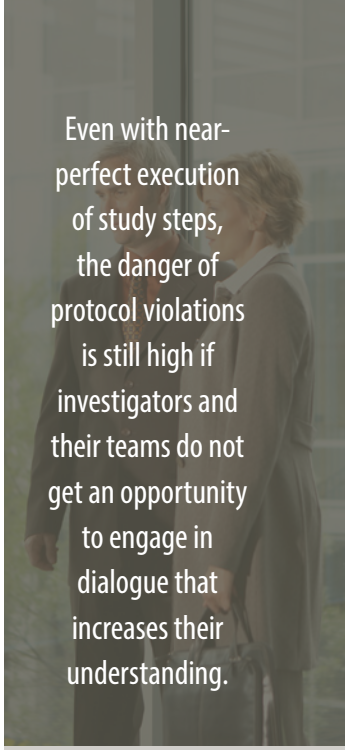
In one study, senior members of the sponsor team decided to go to several sites to walk through the data capture system with investigators and research managers. The meetings turned into full dry runs. The biggest surprise was how simply in-person discussions translated "ah-ha" insights into simple fixes, some of which avoided the unnecessary exclusion of patients. Referencing the engagement model, the research managers became constructively critical Participants in the study community. Some will settle back into an Attendee or even an Observer role, and that's okay. The sponsor hopes some keep their participation level up and that, perhaps, one or two will become Champions.

## Summary

Despite the technical, procedural, and regulatory nature of the clinical research enterprise, the clinical trial is still a long-distance, long-term relationship. The energy people need to play their part to the best of their abilities over long periods of time is sustained by the trust and respect that comes with productive working relationships. Although tools and technology help, ultimately it is the creative energy of a thoughtful study team that inspires people to perform and allows every member of the study community to experience a high-performing, functional team environment. Engagement does not start at site activation, or even the first patient visit; it has to begin with the sponsor study team, long before the study starts.

## Acknowledgments

Much of the content in this article is not specific to clinical research, and is based on the authors' experiences as part of the new work movement known as coworking. Credit for foundational concepts goes to Alex Hillman and Adam Teterus at Indy Hall and Tony Bacigalupo at New Work City. For additional reading, visit http://betterwork.co, http://indyhall.org, and http://nwc.co.

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