SOLVING THE PROBLEM OF CLINICAL RESEARCH ENROLLMENT

DIVE BRANDSTUDIO

A BIOPHARMA DIVE PLAYBOOK

Clinical research is the foundations of modern medical research. Without clinical trials, many promising medical discoveries would never be fully developed and made available to the patients who need them.

Unfortunately, the reality is that a significant percentage of clinical trials today fail to evaluate the endpoints of their studies because of difficulties in enrolling a sufficient number of patients. Many trials shut down early because the investigators are unable to enroll enough patients, or any patients at all. Other trials take significantly more time to enroll patients than expected. This all leads to inefficient research timelines, excessive study costs and costly delays when bringing a product to the market.

Indeed, research has shown that actual enrollment times are typically twice what was planned. And millions of dollars are wasted each year due to these study delays.

What can be done to enroll more patients in clinical trials, increase the operational efficiency of a clinical trial, and decrease the time to reaching the clinical endpoint during trials?

Many pharmaceutical industry experts believe that more data – information about individual investigators and their degree of success in enrolling patients in trials and carrying out protocols – is the solution.

But, perhaps it's more complex than that. In addition to looking at investigators' track records, it would be beneficial to invest in the up-and-coming investigators – those researchers who are moderately successful, the second- and third-tier investigators who, with the right institutional support and perhaps some training, could become first-tier, highly successful investigators.

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In short, we should invest in the less experienced investigators who have the patient population but not the infrastructure or experience, and provide them the tools and education on how to successfully run clinical research trial. This could change the trajectory to a research ecosystem that evaluates study drugs more efficiently, saving time and money. That is the solution that is going to make a difference in your future clinical trials.

— Suzanne Caruso, VP, Clinical Solutions, WCG.

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THE CURRENT CLINICAL TRIAL LANDSCAPE

Taking a step back, let's look at the current clinical trial landscape and today's common problems. How did we get here? What are some of the trends currently influencing clinical trial success?

CLINICAL TRIALS ARE ALL ABOUT TIME.

Every clinical trial sponsor wants their study to move forward in a timely manner. They want to know as quickly as possible whether or not a new compound or device is safe and effective, if it can move onto the next phase of research, and if it will eventually be approved for commercial use and moved out to the market.

That translates into a desire for efficient research timelines. How quickly can a sponsor get a study approved? How quickly can they identify the potential investigators and study sites that are most likely to be successful? How quickly can they ensure that each investigator thoroughly understands the protocol, and gets those sites up and running? How quickly can those investigators recruit, screen and enroll patients? And ultimately, how quickly can the clinical trial reach its study endpoints?

Most study sponsors launch every clinical trial thinking they are going to be very efficient and streamlined. This trial is going to move forward seamlessly, they believe.

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MOST CLINICAL TRIALS DO NOT MOVE FORWARD EFFICIENTLY.

In-house data from WCG and other studies reveal some eye-opening details on the inefficiency of clinical trials.

- Up to 80 percent of clinical trials do not meet their patient enrollment goals or deadlines
- Nearly 20 percent of the clinical trials that were terminated in one year did so because they failed to meet accrual goals
- Across all clinical areas, 18 percent of investigators will fail to enroll a single patient in their trial

In other words, about 20 percent of all the money spent on clinical trials is simply wasted. "Typically, it costs $40,000-45,000 to open one study site," notes Caruso. "Non-performing sites can generate a huge financial impact. It is estimated that nearly $2 billion was spent on non-performing clinical trial sites over a recent 5-year span. That's equivalent to the annual revenue of two blockbuster drugs.

"Clearly, the delay in getting effective products to market can mean billions and billions of future revenues lost."

The bottom line is clinical trial sponsors have a major structural problem. Operations projections are unrealistic unless sponsors are able to start meeting their timelines. As noted earlier, average clinical trial enrollment timelines often double what we expect them to be.

Let's dive deeper into some of the factors that are shaping this current situation.

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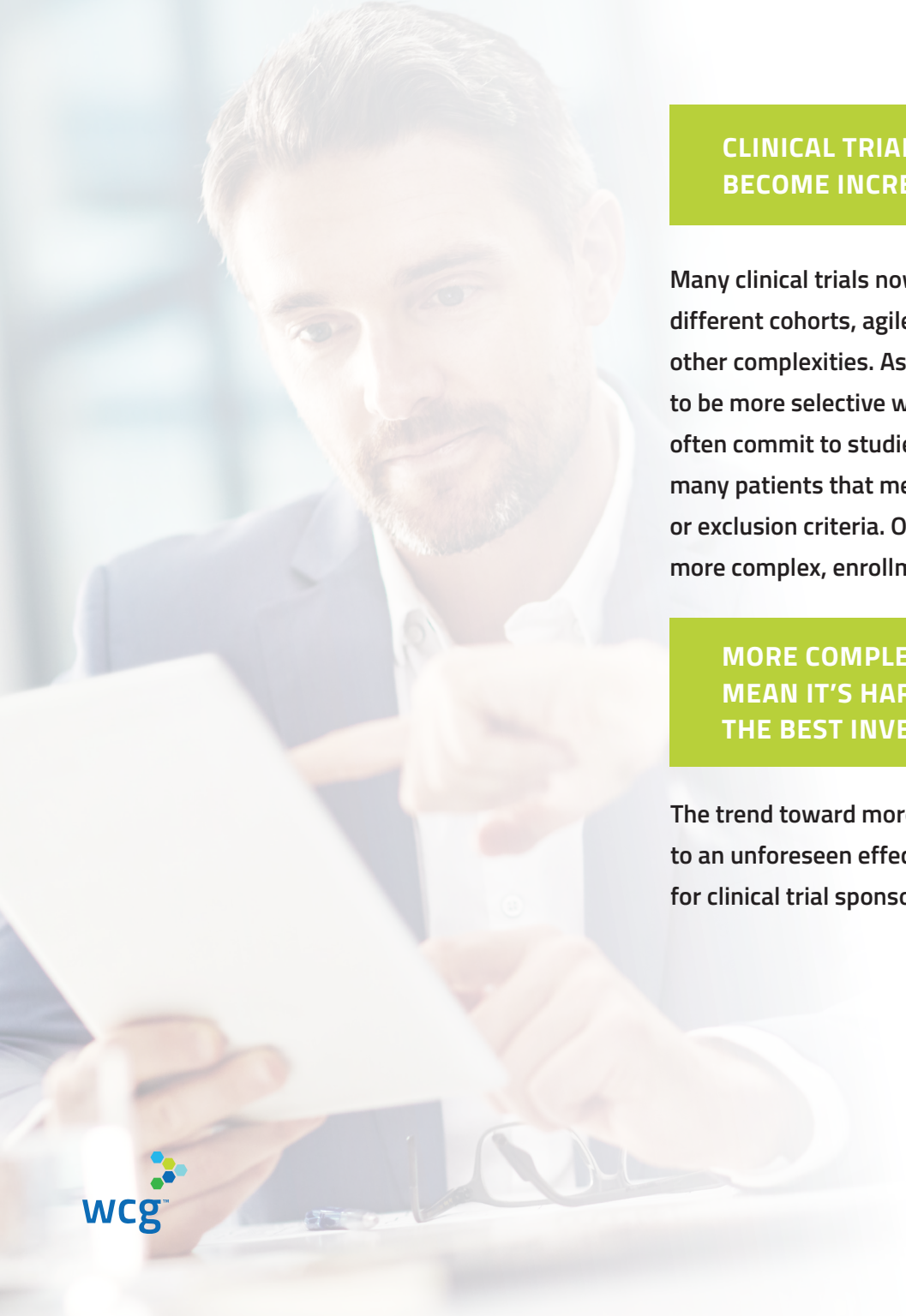

CLINICAL TRIAL PROTOCOLS HAVE BECOME INCREASINGLY COMPLEX.

Many clinical trials now incorporate a number of different cohorts, agile design, adaptive design and other complexities. As a result, investigators have to be more selective when screening patients and often commit to studies where they may not have many patients that meet the clinical trial inclusion or exclusion criteria. Overall, as trials have become more complex, enrollment rates have decreased.

MORE COMPLEX PROTOCOLS MEAN IT'S HARDER TO IDENTIFY THE BEST INVESTIGATORS.

The trend toward more complex studies has led to an unforeseen effect: it's much harder now for clinical trial sponsors to identify appropriate investigators based on their previous clinical trial involvement. For instance, sponsors used to be able to look for investigators who had participated in, say, a lung cancer study. But there are more "basket" protocols now. "Basket" protocols are studies that, rather than looking at a broad therapeutic area such as lung cancer, are studying a specific genetic mutation. Any patient who has that mutation, whether it manifests as lung cancer or breast cancer or another type of cancer, is eligible for that protocol. So, when looking at that pool of investigators, it is not possible to readily identify their area of expertise without additional investigator-specific ancillary information.

In addition, if you look at the records of an investigator who was successful in a broad study a few years ago, it tells you very little about their current capabilities. It's difficult to predict if they would be successful in one of today's more complex studies.

THE NUMBER OF INVESTIGATORS IS DECREASING.

Another factor influencing clinical trial success: the number of investigators participating per trial is decreasing. In 2015, there were about 32 investigators per trial; now it's closer to 17. That means that many sponsors are calling on the same investigators they've used in the past; everyone is vying for the same experienced investigators. As a result, those investigators are becoming incredibly busy, and the pool of experienced investigators available to other sponsors becomes even smaller.

In addition, far fewer new investigators are getting involved in clinical research each year. Looking at the top ten therapeutic areas, there were 3,510 new investigators in 2012. That has decreased each year since, with only 894 new investigators in 2016. This trend will only become even more problematic as older investigators retire, with no one to replace them.

One big contributing factor here is that few institutions currently have programs to train new investigators. Few are willing to invest the time and effort to train a young scientist on how to get involved in clinical research. Many potential investigators don't know how to get involved, especially if they don't have an existing relationship with an academic medical center.

SPONSOR SIZE DOES NOT AFFECT ENROLLMENT.

Many would assume that clinical trials sponsored by large pharmaceutical companies, with their extensive resources, are naturally more successful in enrolling patients than those sponsored by smaller companies. In fact, that is not true. Large pharmaceutical companies, defined as those who sponsor more than 25 studies a year, do not have significantly lower non-enrollment numbers. The numbers are slightly lower, likely because those companies are going back to the same investigators over and over.

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POSITIVE INFLUENCES ON CLINICAL TRIAL SUCCESS

There are two factors that have a positive influence on clinical trial success: investigator experience and site infrastructure support.

Investigator experience clearly is predictive of success in enrolling patients. Looking at data, those who had done four or more studies in the past had non-enrollment rates of about 13%, while those who had done three or fewer studies fared much worse; they had a non-enrollment rate of 25%.

Study site infrastructure is a major factor. Think about a potential site's resources. Does the hospital routinely support clinical trials as part of its daily operations? Or is your investigator perhaps going to spend time doing the background work after his own shift is over? Successful facilities are going to have staff who can spend dedicated time looking for potential enrollees, scheduling those patients and taking them through the screening and consent processes, and enrolling them in the study.

Infrastructure support is often the difference between investigators who do few studies per year and those who do several, and their corresponding enrollment and subsequent randomization rates. Those investigators were supported, and they were trained to become investigators.

THE SOLUTION: IDENTIFY AND INVEST IN THE UP-AND-COMING INVESTIGATORS

The conclusion after analyzing the factors influencing clinical trial success: sponsors need to identify and invest in new investigators, as well as investigators with a tier 2 or 3 track record of enrollment, but with minimal clinical research support.

"As an industry, we need to find those investigators who show promise, who are on the threshold of great success, but are not yet top-tier investigators," says Caruso. "Then, we need to support them, invest in them and give them the resources they need to succeed and move up to become tier 1 investigators."

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What might this support entail?

- Study coordinators who will do on-site medical records research to identify potential enrollees, schedule meetings with them and conduct screenings
- Timely Institutional Review Board (IRB) submissions and approvals
- Timely contracts and payments processes
- Administrative support (data entry)
- Compensation for time spent on study

Finding a service that will provide deep insights into all of these factors for investigators and institutions may afford sponsors the ability to identify potential investigators.

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WHAT TO CONSIDER

Investigator profiles should take into account how many patients an investigator has enrolled in the past, the total number of studies done, the number of studies focusing on a particular mutation and more.

Institutional profiles should evaluate which facilities and departments are the highest-performing, which are likely to be able to take part in an upcoming trial based on experience, IRB timelines, contract turnaround time and much more.

A clinical trial knowledge base should assess protocols in every therapeutic area, evaluate relationships among sponsors, contract research organizations and study sites, evaluate study design, and contain enrollment performance data on FDA-regulated investigators.

Sponsors looking for clinical trial investigators should not limit their search to the high-performing investigators who are currently in demand. Rather, they should start by determining the most important attributes needed in an investigator pool. For instance, maybe your investigators need to know how to do a certain test. Or maybe you need investigators who have experience in a particular protocol design. Or perhaps you just need an investigator who sees 400 patients with a particular profile each year. Consider adding other predictive features or key criteria to that profile, such as their ability to enroll a certain percentage of patients compared to their peers.

A good approach would be to find the investigators who perhaps don't have as much experience as those in high demand, but who are highly likely to deliver the patient enrollment results you need. Look for the investigators who have decent numbers but are right on the threshold of being even more effective.

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Add to that insights about those investigators' institutions: are they supportive of research, do they have efficient IRB and contracts processes? This information can be organized and analyzed to identify the best potential investigators for your study.

If clinical trial sponsors take the time to find these up-and-coming investigators, invest in them, and give them the support they need, research timelines will become more efficient. We will be able to deliver life-saving medications and devices to patients even sooner.

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But support for your study should not end there – there should be a rapid and seamless activation of clinical research sites through feasibility, contracts and payments services. From there, an effective service should work with your sites through patient engagement services to ensure they meet or exceed their enrollment times.

Using a service that offers a database, as well as expert insights, sponsors will have access to a high-performing pool of investigators for an upcoming trial, significantly decreasing the time needed to meet patient enrollment targets.

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