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Data-Driven Approaches Accelerate Trial Recruitment AND QUANTIFY RISK

At one time, biopharmaceutical companies could develop their clinical trial recruitment strategies using nothing more than historical experience, anecdotal knowledge, and gut instinct. They could trust investigators to supply the necessary patients, and as a last resort, bolt on some media coverage. But, that cottage-industry practice no longer works. To find patients and consistently complete trials faster, sponsors must now regard patient recruitment as an essential part of the "trial DNA." By leveraging data and predictive analytics, companies find patients and know how to reach them. In this model, success becomes so predictable that a recruitment services provider can base its cost on the actual value created — rather than on enrollment quotas or, worse, on executing a set of recruitment tactics.

The Call for a Radically Different Approach

The biopharmaceutical industry has been challenged to accelerate product development in part because the clinical trial process begins with a faulty assumption (sites will supply the patients we need) and in part because recruitment is managed sequentially (we'll try something else if sites don't deliver). The fact is, sites rarely deliver what sponsors expect in the allotted time; 37% of sites fail to meet their enrollment targets and the original timelines for Phase II-IV studies usually end up doubling.

So, trial timelines — and market entries — have been held hostage by delegating patient recruitment to sites as the standard "Plan A." This translates into millions in added operational expenses and lost opportunity costs.

Other industries have used data-driven insights to guide dramatic productivity improvements and generate superior business results. Southwest Airlines used data on travel patterns to inform its pricing strategy and remain profitable, while most others in the industry were struggling. It's time for clinical development organizations to also use data and analytics to drive a consistent set of business practices — practices that can minimize recruitment time and ultimately get products to market sooner.

Rather than applying recruitment tactics sequentially, it is far more effective to develop a targeted recruitment strategy as an essential component of the trial plan — and then employ multiple tactics in parallel. The key is to use information, analytics, and technology to good advantage in setting the right strategy.

Figure 1: Probability of Success without Patient Recruitment

Without a patient recruitment campaign, there was an 85% probability of successfully completing the study enrollment in 12 months

Probability of Success	Enrollment Period
50%	7.001
55%	7.353
60%	7.783
65%	8.204
70%	8.704
75%	9.434
80%	10.476
85%	11.997
90%	17.063

Preliminary Research

Today there are many rich sources of data that can inform the recruitment plan, as well as sophisticated statistical tools to test various what if scenarios and establish confidence levels for the results. Three main tracks of research should be undertaken before the trial plan is set:

- The first step is to estimate how many patients are eligible to participate. The inclusion/exclusion criteria can be analyzed against data in electronic medical records (EMRs) and pharmacy or integrated medical claims databases to determine the proportion of patients that meet the criteria and to pinpoint where they're located.
- The next step is to zero in on those sites that have the ability to deliver the most patients. It is possible to use a combination of publicly available databases on sites' locations to highlight those in close proximity to clusters of patients who match the inclusion/exclusion criteria. Then, a commercial database that scores investigators objectively on their past enrollment performance can be used to select the best ones for the study at hand.
- Simultaneously, primary research should be done to understand the patient's perspective on the trial. Trial planners should explore how the target patient population would respond to the protocol requirements. What would they find appealing or objectionable about the approach? What motivational drivers would influence their participation decision?

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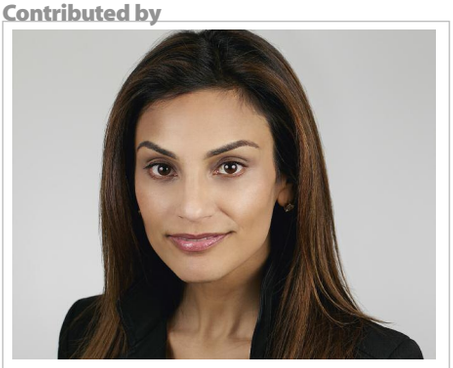

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"Surround-Sound" Recruitment

For the most part, sponsors and CROs have provided sites with small advertising budgets to use at their discretion in raising patient awareness of trials; they've used no overarching strategy or coordinated campaign. However, recruitment programs conceived and managed centrally can be vastly more effective in allocating dollars across media and ensuring that the messages used will resonate with patients, caregivers, and referring physicians.

The toolkit of available tactics, which should be tailored to the needs of each individual trial, include:

- Digital platforms and social media campaigns to drive traffic to physicians and websites for trial information
- Patient awareness and support materials distributed through physicians and pharmacists

Figure 2: Probability of Success with Patient Recruitment

Probability of Success	Enrollment Period
65%	5.85
70%	6.111
75%	6.471
80%	6.962
85%	7.622
90%	8.704
95%	11.116

- Partnering with advocacy groups and patient communities to place trial ads on websites, Facebook pages, and other online resources
- Engaging key opinion leaders as ambassadors of the study
- Traditional broadcast media

Determining how to allocate resources across these channels involves extensive analysis of media reach, audience profiles, and performance benchmarks, making the outreach plan very data-driven.

Predicting Success

Ideally, recruitment campaigns should be considered when sponsors are creating their trial plans, forecasting enrollment timelines, and building their budgets. But, how can the value of future campaigns be determined?

The answer, once again, is to draw upon data and to apply analytical tools to aid in decision making. A historical analysis can reveal the impact of campaigns conducted for studies on analogous products. One can then use statistical modelling to estimate the cost and time required to randomize the required number of patients. The results can be displayed as a chart showing the probability of meeting enrollment targets under each scenario.

A Proven Approach

Following are two cases demonstrating how data and analytics can inform the recruitment process, shortening enrollment periods and delivering operational savings.

Accelerating Recruitment within a Seasonal Window of Opportunity

For one company conducting a Phase III study, time was running out to enroll patients before the recruitment process would have to be put on hold for a year due to seasonal aspects of the protocol. To accelerate recruitment, the sponsor launched a patient recruitment campaign that immediately delivered results. After just 12 weeks of advertising at a cost of $612,000, sites had enrolled 280 patients. Had the sponsor not launched the campaign and continued recruiting at its earlier pace, it would have taken an additional 23 weeks to recruit the same number of patients. By shortening the recruitment timeline by nearly six months, the company was able to save more than $4 million in operational costs alone.

Planning Enrollment Targets with Confidence

In another Phase III trial, a company aimed to have 200 patients randomized in eight months using 25 sites. In actuality, it ended up needing 11.5 months, even after adding 8 rescue sites for a total of 33. Analysis using enrollment modeling demonstrated that even with a different set of 29 high-performing sites, there was an 85% probability that enrollment would have taken 12 months. **(See Figure 1.)**

However, had the company also run a coordinated recruitment campaign, the outcome would likely have been quite different. A statistical simulation revealed that there was an 85% probability of successfully enrolling the required 200 patients in just 7.6 months by spending $750,000 on a direct-to-patient recruitment campaign. In shortening the enrollment period by 4.3 months, the company could have saved $1.5 million in operating expenses alone, making the net return on its investment in advertising $750,000. **(See Figure 2.)**

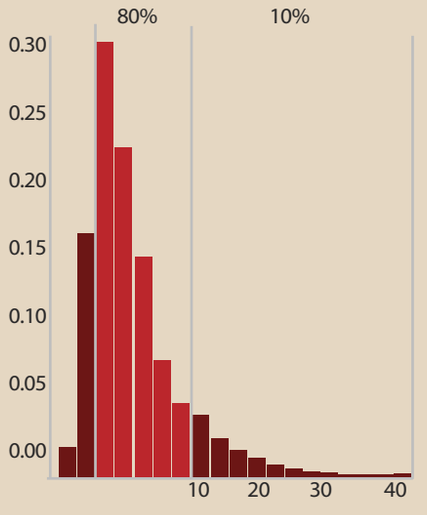
A Shift to Outcomes-Based Pricing

Traditionally, pharmaceutical companies have contracted with CROs on a transactional, fee-for-service basis. Two factors, however, are serving as catalysts to move sponsors from contracting on the volume of work CROs perform to the value they deliver. First, the industry is under tremendous pressure to bring products to market faster, such that time itself is a commodity with a specific value. Second, thanks to the predictive analytics described here, it is possible to know from the outset and with great certainty what the return on investment will be for specific recruitment services.

In helping sponsors forecast enrollment timelines, select the best sites, and reach and engage patients, the latest information and clinical service innovations also deliver value by:

- Providing a better understanding of the patient population, which guides product development and ensure a competitive advantage at launch
- Supplying insights into patient behaviors that can inform the commercial strategy
- Optimizing future trial designs, with expedited clinical trial recruitment

Wouldn't a pricing model based on the value of the recruitment services — to encompass time saved in the recruitment cycle — be more aligned with sponsors' overall objectives than one based simply on the number of patients referred or enrolled or even less meaningful, based on executing a set of recruitment tactics? Meeting patient enrollment targets is, after all, simply a means to an end: completing trials expeditiously in support of a successful product launch.



Y axis = Density

X axis = Enrollment Period in Months

With the addition of a centralized patient recruitment campaign, there was the same probability of achieving success 4.3 months sooner.

In Conclusion

Sites' inability to meet sponsors' recruitment needs has become a major roadblock in the clinical trial process. It's time for sponsors to manage the process differently by adopting proven, innovative, data-driven best practices from other industries to assess the trial landscape, better evaluate sites, gain insights on patients, and develop recruitment plans accordingly.

Using evidence-based decision-making, building a comprehensive recruitment strategy into the trial DNA, and adopting value-based pricing will require a commitment to innovation; but it will not require blind faith. The science is established and proof is available. PV