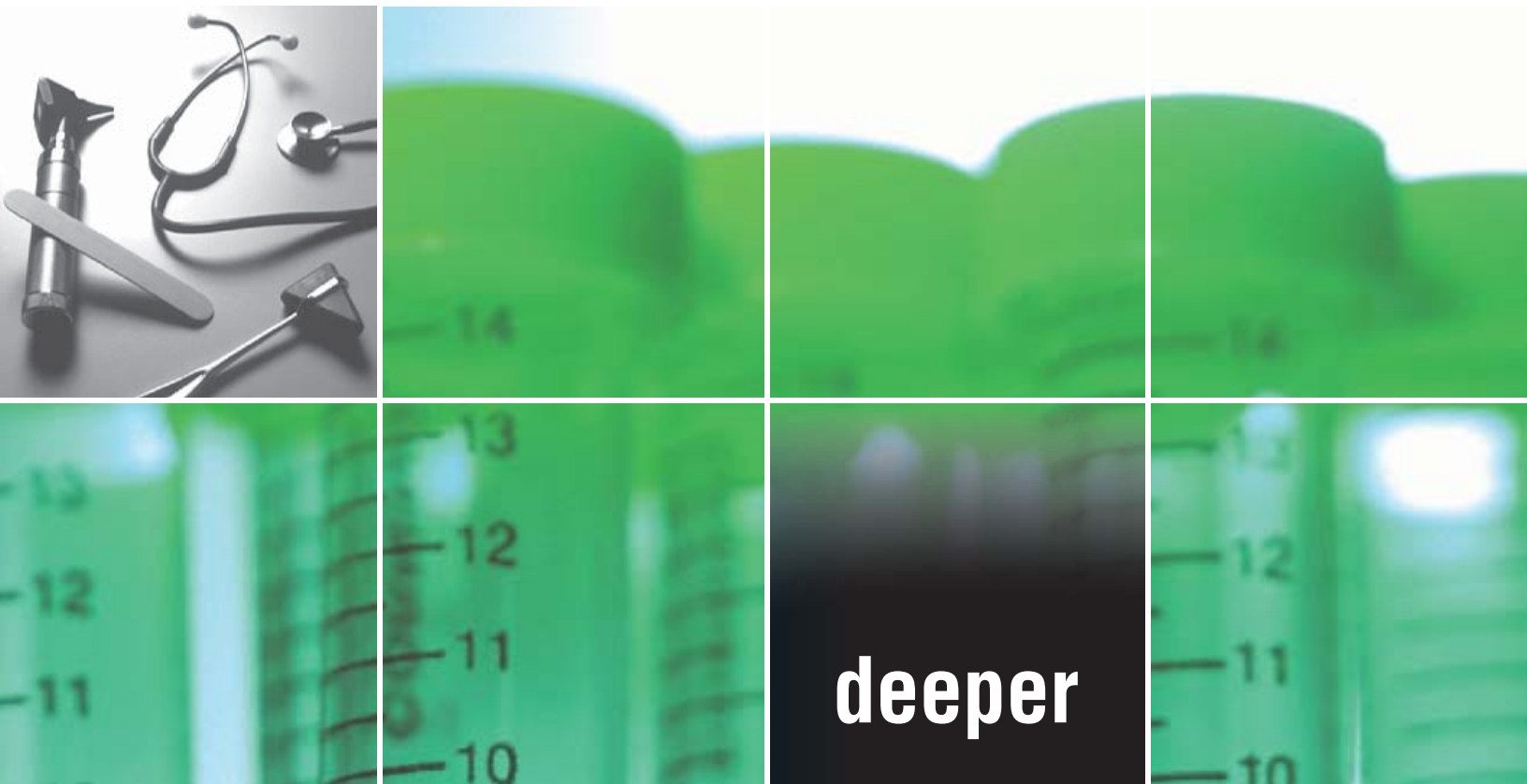


Delay no more: Improve patient recruitment and reduce time to market in the pharmaceutical industry



An IBM Institute for Business Value executive brief

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Delay no more: Improve patient recruitment and reduce time to market in the pharmaceutical industry

With increasing industry pressure to develop, test and market greater numbers of new drugs faster, pharmaceutical companies need to perform clinical trials as quickly as possible. Inefficient patient recruitment processes will increasingly become a formidable barrier to pharmaceutical companies' success in launching new products. Improving the patient recruitment process is imperative to avoid wasted investments and eliminate costly delays in bringing new drugs to market – today and even more so in the not-so-distant future.

Patient recruitment pains: Is there a cure?

Patient recruitment is a critical issue as increased industry pressures threaten profits for pharmaceutical companies. Though patient recruitment consumes 27% of the cost of development¹ – that is US\$5.9 billion annually around the world² – only 1 in 20 recruited patients provides results that can be included in a regulatory dossier.³ The difficulty that most pharmaceutical companies face in recruiting and retaining patients is a major cause of clinical trial delays. In fact, over three-quarters of all clinical trials currently fail to meet their recruitment deadlines.⁴ Delays mean new drugs can't get to market, which can result in lost profits.

Improved patient recruitment presents one of the largest opportunities for pharmaceutical companies to eliminate delays in clinical trials, thereby making it possible to reduce time to market. Researchers at the IBM Institute for Business Value assessed current industry practices in patient recruitment. They focused on the most effective approaches to patient recruitment, the motivating factors for physician and patient participation and the capabilities required to successfully and efficiently complete a patient recruitment program. The resulting study concluded that by focusing on increasing the pool of available patients, retaining participants, improving the ability to utilize retained patients in subsequent clinical trials and improving knowledge sharing across corporate boundaries, pharmaceutical companies will substantially improve the patient recruitment process.

Trials in the pharmaceutical industry

Over the last two decades, growth in research and development expenditure in the pharmaceutical industry has significantly exceeded that of sales.⁵ But despite the continual rise in costs, time to market has not decreased. Because pharmaceutical companies are targeting more diverse populations and multiple therapeutic areas, clinical trials have become more complex and costly – a trend that is likely to escalate. New regulatory requirements have increased the number of patients, procedures, and trials per New Drug Application (NDA)/Market Authorization Application (MAA) submission, which has also contributed to the complexity of patient recruitment.



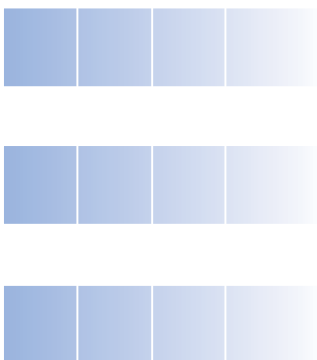
**"There is an inability on the part of pharmaceutical companies to anticipate the time involved in the recruitment process. For example, when they will spend investigator fees, which can be months or years off. As a result, companies tend to over-allocate people and wind up with people sitting idle. The whole process becomes gummed up."
– VP Sales, patient recruitment software company**

Troubling patient recruitment issues riddle the clinical development process from beginning to end. Current pre-trial planning is inadequate: feasibility studies are often flawed – or absent – and past performance data is not properly utilized to support feasibility assessments. Also, recruitment strategies are underdeveloped, ad hoc in nature or nonexistent. The pre-trial planning process is often siloed internally across the value chain – in most companies, collaboration among key departments such as discovery and marketing is not a common practice. Investigator data is not shared, resulting in the reuse of poorly performing sites. Performance metrics are few to none. Overall, pre-trial planning is reactive rather than proactive, with little or no contingency planning.

In addition, variables such as a poorly defined product development strategy, failure to take into account different medical practices for international, national and regional studies, the skill levels of clinical development staff, and project management capabilities threaten the success of clinical trials. Finally, pharmaceutical companies are often challenged by a lack of financial and personnel resources as well as inadequate physical space to conduct trials.

The next step in the clinical trial process, protocol design, is often based on demanding and often unrealistic forecasts that may not adequately reflect patient populations. The forecast can be distorted if market research is not used to sufficiently understand the patient population, and patient populations are not tracked to validate protocol assumptions. The types of patients described in protocols often do not exist in reality, and inclusion and exclusion criteria may be too stringent to allow the required number of participants. Overly demanding protocols often lengthen trials, and then require modifications that can lead to even further delays.

Practicing physicians are currently inadequately involved in protocol development, as pharmaceutical companies rarely go to the field for feedback on the protocol design. Frequently, only key opinion leaders – the few academics at the top of the pyramid – have input into protocol review. These leaders are often specialists who see highly specific patient types, so their opinion on patient availability for specific conditions can be skewed. However, their status and their importance to the marketing efforts of pharmaceutical companies make them hard to bypass. And while the role of Clinical Research Coordinator (CRC) is critically important in taking the pressure and workload from clinicians, it is uncommon for CRCs to provide feedback on protocol development – if they do, it is often too late in the process.



"Involving PIs up front would help get their buy-in by making sure that they are well educated about the protocol. Also, having lunch or dinner meetings to keep them involved and interested – stage reminder events and communications and provide them with cheat sheets."
– Clinical Study Manager, top tier pharmaceutical company

"If we could get as much of the good things that come out of clinical trials publicized as opposed to the bad things, we could make a lot of progress. I would love to see industry behind this in conjunction with researchers and regulatory agencies – everyone as a team helping the public understand the good things that come from clinical trials."
– Clinical Research Director, university research unit

Principal Investigators (PIs) have significant influence on the availability of suitable patients for clinical trials. The commitment, attitude and involvement of PIs directly affect the cost and time required for patient recruitment, as well as the quality of clinical trials. But qualified PIs are hard to find, and confirming the probability of success with PIs is often difficult. Pharmaceutical companies have no way of knowing if the PI can conduct the trial and deliver results within the defined time frame; PIs are often overly confident and then can't deliver the promised patient population.

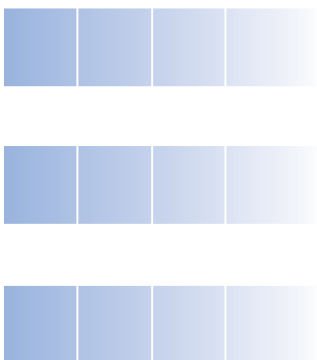
Although the PI is invited to study seminars and training in preparation for the clinical trial, other essential staff – such as site staff, pharmacists or CRC – may not be. This can cause subsequent delays because key staff members do not have access to the appropriate information. Finally, qualified PIs are hard to keep: their satisfaction, after participating in clinical trials, is often low. Since currently there is little or no effort on the part of pharmaceutical companies to coordinate and leverage the relationships with PIs they have recruited in the past, the relationship falls away after the trial is completed.

While the PI's role in recruiting patients is inarguably crucial to clinical trials, patients are increasingly educating themselves. Thanks to an abundance of information, patients are more proactive and knowledgeable about their treatment options than ever before. Patients learn about trials through traditional and online media; however, what they learn is often negative. Media coverage typically focuses on damaging aspects of clinical trials – patient mistreatment, unethical practices and process shortcomings. A recent study reflects that 79 percent of adults are reluctant to participate in clinical trials because they felt research participants were taking a gamble with their health.⁶ Misunderstanding and lack of awareness are largely a result of the complexities and limitations of clinical trial advertising. In lieu of straight-forward information on the benefits of clinical trials, negative press is powerful and can cause patients – and physicians as well – to edge away from clinical research.

From trials to triumphs: Patient recruitment Rx

Research shows that out of 20 patients identified for a clinical trial, only one will participate long enough to provide data that can be used in a regulatory dossier.⁷ That's quite a reality check for pharmaceutical companies, who face many challenges in their race to market with new drugs.

Pharmaceutical companies need to increase the pool of available patients for clinical trials and, more importantly, retain them. At the same time, corporate processes must be aligned to enable companies to best access patients and prospective participants, as well as utilize them in subsequent trials. Finally, successful contenders in the pharmaceutical industry will be those who realign



internal processes to gain speed by avoiding the "rework" that is typically a result of inadequate knowledge sharing within the company. The IBM assessment of the pharmaceutical market yielded the following key challenges and potential solutions for pharmaceutical companies in their quest to optimize patient recruitment:

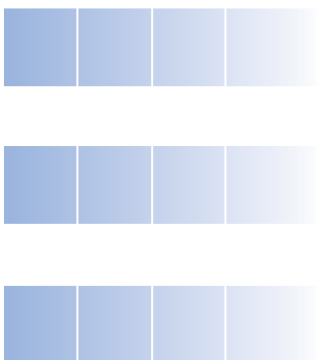
Challenge:	Improve the image of clinical trials
Solution:	Build an industry alliance to improve the profile of clinical trials

An industry alliance is the most feasible administrative structure to gain positive national publicity for clinical trials. However, an industry alliance proposed to "transform trial recruitment by the end of 2002" has still to deliver results.⁸ The consortium set out to improve relationships with physician investigators, address the inherent limits of the informational role of the National Institute of Health (NIH) and build public awareness of the legitimate reasons behind rising drug costs. As of today, that vision has not yet materialized and the challenge to create an effective industry alliance still stands.

While an alliance led by a designated, neutral research organization promises the fewest conflicts and the highest chance of success, the main question in the development of an industry alliance is who will take the first step to act as a preliminary alliance administrator. The organization to take the first step will likely be one that stands to benefit significantly from improved patient recruitment and improved public perception in a given therapeutic area. The "first mover" will incur the costs and time associated with promoting plans to other potential members, as well as the risk of exposing sensitive competitive information as they make the case for action. However, their status will no doubt allow them to define the terms of any agreement of a newly formed industry alliance.

Challenge:	Increase the pool of patients for clinical trials, and then retain them
Solution:	Enhance internal marketing and screening capabilities

Improving the marketing management capabilities in R&D is essential to market to a targeted population of prospective patients. Pharmaceutical companies must determine what they know about clinical trial participants today, how efficiently and cost-effectively that information is captured, stored and used, and whether current data is useful for analysis.



The cost of retaining a subject is as little as one-fifth of the cost of recruiting a new subject.⁹ That is why optimal screening and retention procedures – for both PIs and patients – are imperative to effective patient recruitment. PIs must fully understand the dynamics of screening (even where patient population is available, drop out rates can be high) and must be armed with clear protocols for trials. Everyone from PIs to call center staff must have a clear understanding of inclusion/exclusion screening criteria for the trial.

Effectiveness of retaining patients in a clinical trial should be analyzed according to specific trial variables: how long were the studies, what were the patients' concerns, were patients interacting with unfamiliar PIs or their own doctor, was the patient in the placebo group? Pharmaceutical companies should also measure the current screening and retention performance of their vendors and contract research organizations (CROs) to set a baseline for success.

Challenge:

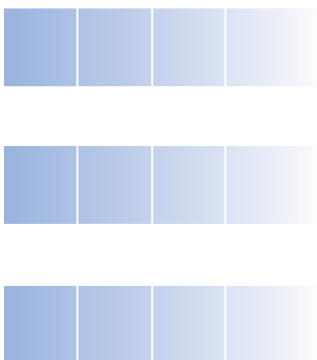
Improve access to the patient pool

Solution:

Develop a robust approach to investigator relationship management (IRM)

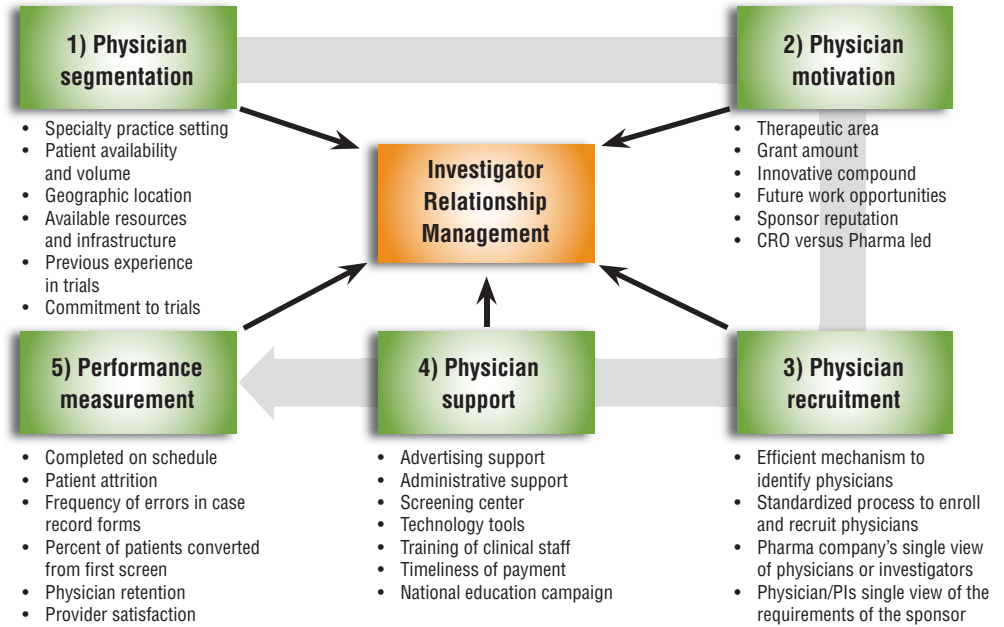
The most cost-effective route to recruiting PIs is to retain and reward those who consistently deliver high numbers of patients, are committed and have the necessary resources and infrastructure to support clinical trials. However, by focusing solely on current performers, pharmaceutical companies can miss a larger pool of potential PIs with good access to targeted patients. Doctors are the closest link to patients: training new physicians to be PIs provides pharmaceutical companies with additional avenues to targeted patient groups. Untrained physicians may shy away from clinical trials for fear of losing patients by referring them to sites. However, training can be expensive and new doctors' lack of knowledge, experience, resources and infrastructure can be stumbling blocks to the success of their initial trials.

International expansion to recruit PIs extends the pool of potential patients considerably. Regulatory authorities have eased restrictions on clinical trials overseas, and PIs are amenable to participation, viewing clinical trials as an additional source of income. Access to broad patient populations, in Asia for instance, presents pharmaceutical companies with much needed opportunities to increase the patient pool. In addition, clinical trials offer valuable access to healthcare and medicines in less developed nations. However, the costs to monitor these trials are greater, and regulatory requirements can sometimes nullify patient data gathered from these nations. Ethical issues – such as the population's limited ability to purchase the drug they tested once it is approved – need to be considered as well.

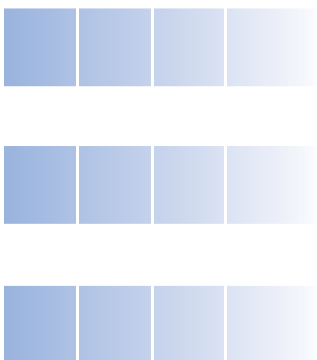


To make the most of their physician relationships, pharmaceutical companies need to employ a physician-centric Investigator Relationship Management (IRM) model (see Figure 1), where insights into physician segmentation, motivation, requirements and performance metrics are systematically collected and used to enhance the overall physician experience in conducting trials.

Figure 1. Five steps to successful Investigator Relationship Management.



The benefits of IRM are many. Physicians can communicate more easily with sponsors, and receive valuable information from pharmaceutical companies, such as account payment status and information on future trials, as well as maintain a physician profile. Sponsors are provided with better and more timely communications about protocol updates and amendments. The ability to maintain long-term relationships with PIs is enhanced. In addition, pharmaceutical companies can do a better job of profiling and rating PI performance and implement more effective marketing campaigns for future trials.

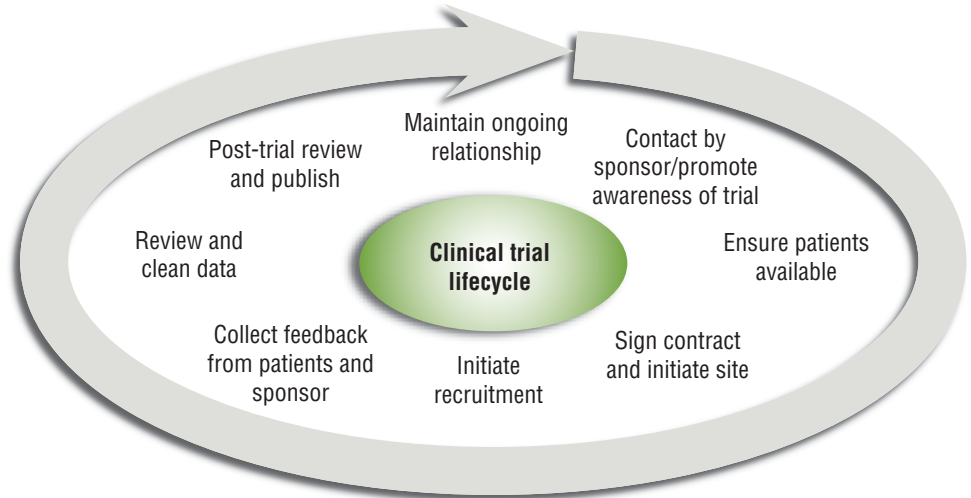


Challenge: Align internal processes to increase the company's ability to utilize the patient pool in multiple clinical trials

Solution: Adopt an integrated approach to patient recruitment management

To retain as many enrolled patients as possible, the pharmaceutical company must integrate the patient recruitment process across the entire clinical trial lifecycle (see Figure 2).

Figure 2. An integrated approach to patient recruitment management.



Resources dedicated to patient recruitment benefit from process, organizational and technological changes, such as improved training for recruitment personnel, incentives for recruitment managers based on timeliness, and implementation of reporting technologies to provide regular usable recruitment data (see Figure 3). PI recruitment should be focused to bring in physicians with targeted treatment specialization and demonstrated patient recruitment skills. New training to improve PI and CRC recruitment skills, marketing messages targeted to PIs' interests and experience and the implementation of technologies designed to facilitate training and feedback from PIs are a few examples of steps that can be taken in an effort to recruit and retain highly desirable PIs.

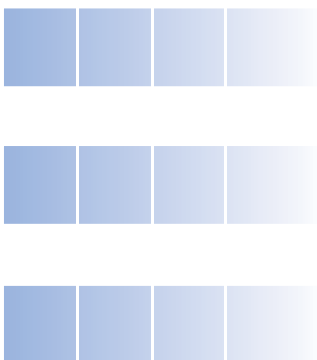
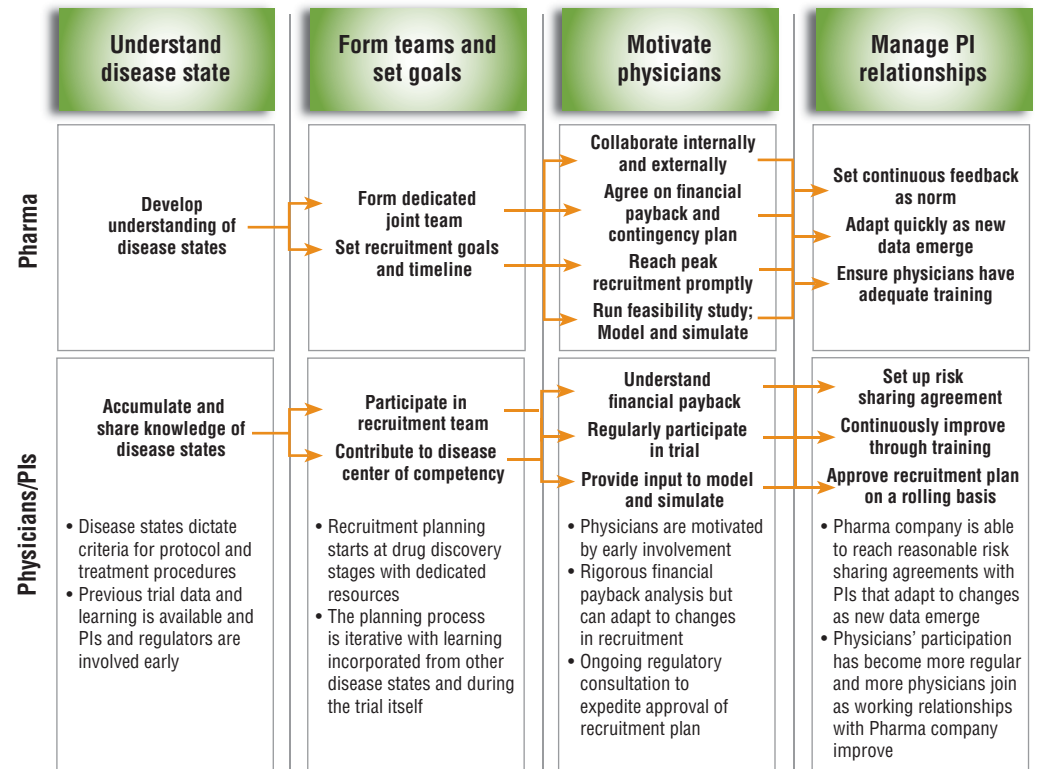
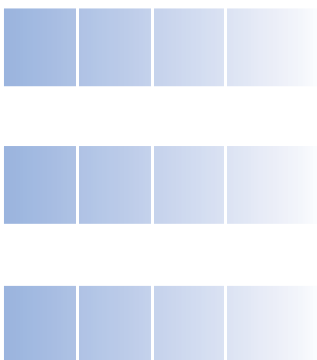


Figure 3. An integrated process approach enables each key step of patient recruitment for both pharmaceutical companies and principal investigators.



In the pre-clinical trial stage, the first step is to build a dedicated team responsible for patient recruitment that establishes objectives, builds a project plan and involves both discovery and marketing at an early stage. The most accurate plans are based on a firm understanding of the disease and the patients to be targeted, as well as securing leadership buy in. Metrics for success should be set with rewards for timeliness and adherence to the trial budget.

Pharmaceutical companies should form recruitment strategies for each trial based on an evaluation of historical performance data on each recruitment channel, the criteria for a centralized or local ad campaign and the best mix of media channels. Key considerations in forming recruitment strategies are the recruitment goals, site characteristics, patients and budgets. For example, who are the patients targeted for the study, how many sites will be involved in the protocol and what is the ideal patient accrual timeline?



In the protocol design stage, making protocols more realistic and improving the feasibility testing of protocols will go a long way toward improving patient recruitment. Revamping the protocol review process to enable the early involvement of PIs and CRCs will benefit these goals. An adequate and realistic assessment of the time needed for input and feedback is also crucial. Lastly, pharmaceutical companies must build a foundation for more transformational process changes in the future: as the complexity of the market compounds, so will the necessity for increasingly efficient and proactive protocol design processes.

Developing a contingency plan for clinical trials allows for the management of risk and delays. Contingency strategies should cover unexpected impacts on budget, sites, PIs, clinical staff, patients and advertising plans. If pharmaceutical companies have a backup plan in case, for example, more patients drop out than expected or sites are added or withdrawn, then they will be better prepared to stay on track, keep to timelines and perform within budget.

If implemented correctly, an electronic forecasting capability can create a more accurate, iterative patient recruitment process that can speed clinical trials – and reduce time to market for new drugs. However, it should be stressed that pharmaceutical companies would do best to model potential payback prior to engaging in any recruitment program to help gauge the proper investments in process, organizational and technology changes. The progress of implemented programs should be measured carefully and often; individual incentives and responsibility should be tightly linked. It is paramount that financial expectations are communicated to all involved players and that performance analysis technologies are employed to provide a realtime, ongoing assessment of recruitment effectiveness. The integrated approach to patient recruitment should increase the efficiency of each step of patient recruitment, for both pharmaceutical companies and PIs.

Challenge:

Use intellectual capital and data from previous trials to save time and gain competitive advantage

Solution:

Formalize the learning and knowledge-sharing process across the entire clinical development environment

To remain competitive, many organizations are harnessing the "learnings" from previous projects to increase overall efficiency, cut down on duplication of tasks and errors and facilitate a more proactive working environment. Improved organizational learning and knowledge sharing can offer pharmaceutical companies increased competitive advantage: if pharmaceutical companies were to capture, store, and reuse data from clinical trials across the value net from R&D to patient recruitment to sales and marketing, they could shave precious time off of the race to market with new drugs.



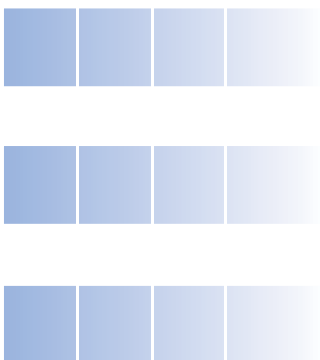
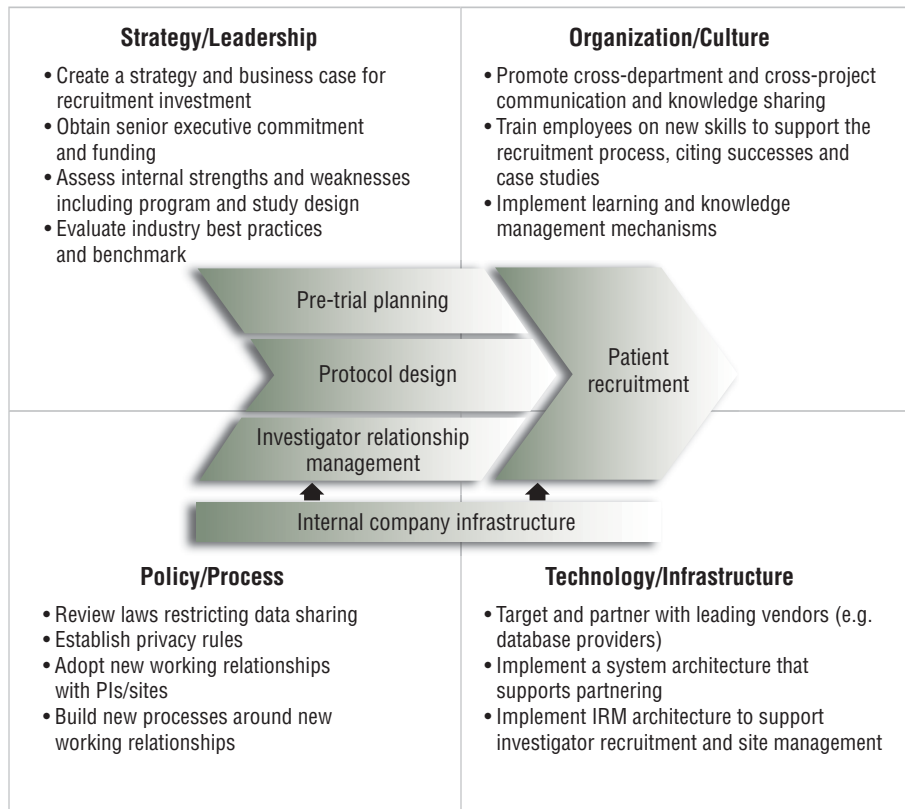
"You reinvent the wheel almost every time you do a study...it would be of real value if the sponsors could do some of that work in advance."

– Clinical Research Director, university research unit

A team-based work environment can drive process efficiency. Pharmaceutical companies should create joint teams where possible to determine how both strategic processes and networks of partners across all service areas and geographies can be better integrated to support the recruitment goals. Incentive programs should be designed to encourage collaboration across the organization.

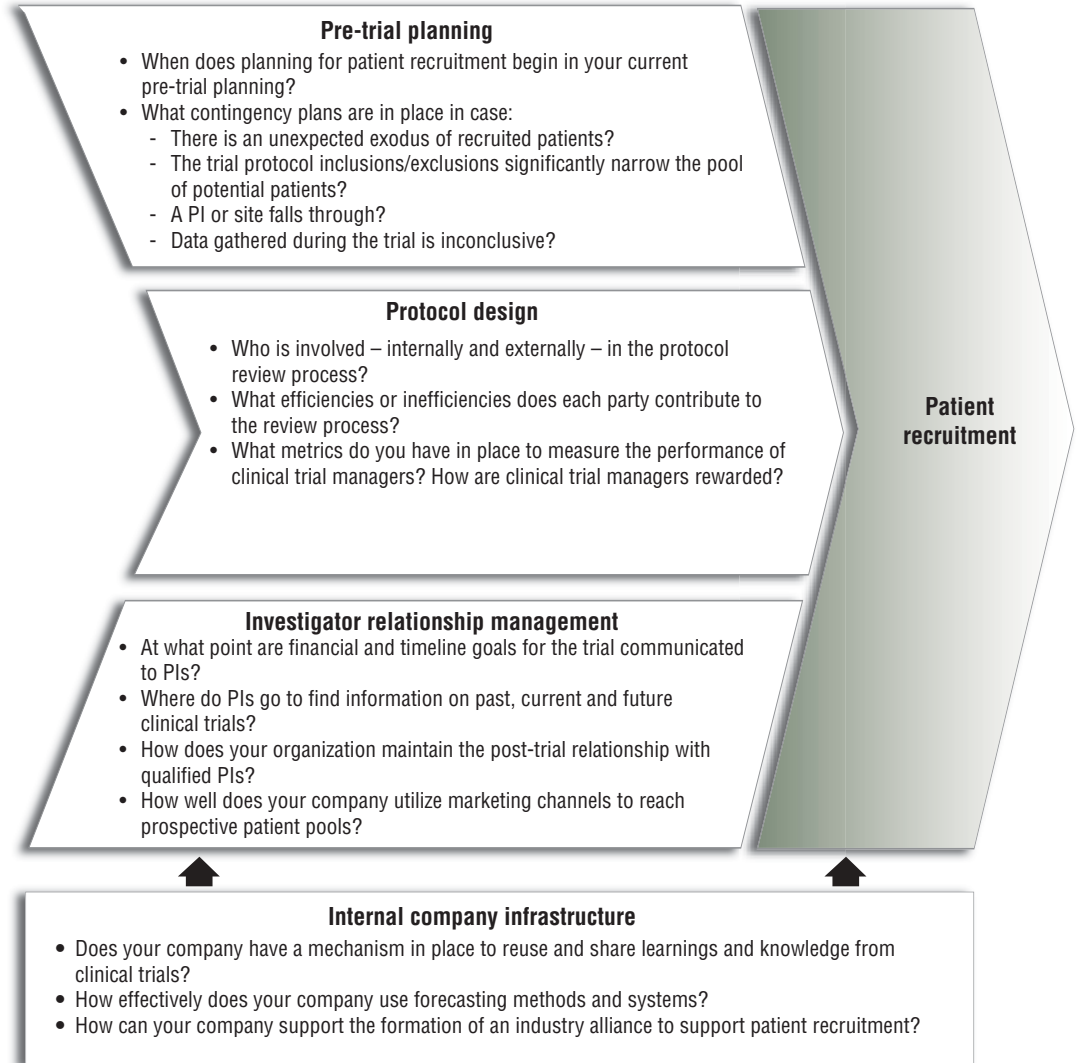
By harnessing and sharing detailed data concerning patient recruitment, PI specialization and performance and clinical trials, pharmaceutical companies can reap the rewards of past projects, rather than starting each clinical trial from scratch and risking the repetition of past mistakes. A roadmap to improved organizational learning and knowledge sharing illustrates best practices pharmaceutical companies should consider to begin the process of better utilizing organizational knowledge (see Figure 4).

Figure 4. Four critical aspects of 'best practice' patient recruitment processes.



The path forward

While some pharmaceutical companies are on their way to alleviating the pain from inefficient patient recruitment, most companies may find they face a long journey to create more efficient patient recruitment processes. The following questions are designed to help pharmaceutical executives assess their current processes and begin to chart a path forward.



Conclusion

Time is money in the pharmaceutical industry. Delays in clinical trials keep pharmaceutical companies from their essential goal: being first to the marketplace with innovative new drugs. When patient recruitment is inefficient, valuable investment expense is wasted and precious time is lost – as are potential profits and competitive edge.

As clinical trials for new drugs become more complex, pharmaceutical companies must recruit increasingly diverse patient populations in larger numbers. And pharmaceutical companies will not be able to effectively target these large patient populations without considerable improvements in two main areas: recruitment of PIs and improving public perception of clinical trials.

Pharmaceutical firms must also focus on retaining the patients and PIs they do recruit. Instead of seeing patient and PI recruitment as a static process with a beginning and an end, pharmaceutical companies should adjust their views, as well as their processes, to support recruitment as an iterative process. Patient recruitment should be fully integrated in clinical trial planning from the very beginning. PI recruitment, as well, will benefit from a physician-centric IRM model that focuses on improving the relationship with PIs. Last but not least, pharmaceutical companies must begin to see their knowledge and data gained from past clinical trials as an invaluable asset in gaining a competitive edge and align process, organization and technology to harness and reuse information to shave time off future trials.

In an environment of constant change, planning for contingencies in patient recruitment is vital. Only companies that are quick on their feet will get the patients, PIs, and trial data they need to get to market, while staying within budget – without delays. It doesn't happen without focus. To explore the ways in which we may assist you in improving patient recruitment, contact us at iibv@us.ibm.com. To browse other resources for business executives, visit our Web site:

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08-03
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