

Adaptive Site Performance Management

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In any research study, some sites will perform well, some average, and some poorly. It is common for study sponsors to try to help underperforming sites improve their performance. However, this rule for allocating assistance is too simplistic. A better allocation rule would evaluate sites in three dimensions:

- How well is the site performing?
- Is the sponsor able to help the site perform better?
- Is the site willing and able to improve performance?

A small amount of assistance may help a high-performing site perform even better. On the other hand, all the assistance in the world will not help a site that does not want any help or cannot implement changes.

This article will focus on subject recruitment performance, but the principles are broadly applicable. There are four primary ways for a sponsor to help a site improve its subject recruitment performance:

- Consult with the site to identify and remedy problems.
- Train study personnel in subject recruiting techniques.
- Motivate the site to apply more of its resources to the study.
- Provide additional resources such as advertising dollars.

It is not enough to know that subject enrollment is behind schedule; the causative factors must be determined. For example, the study coordinator may be tied up with another study. The site may not be aware that billing records can be mined for ICD-9 diagnostic codes. The site may be looking for subjects in the wrong places. The recruiting materials may be held up at the IRB. The site monitor can consult with the site to identify and remedy such problems.

Training can be very effective with sites that are unskilled at subject recruitment. Training topics should be selected to meet the needs of the site. There are various ways to deliver training, such as one-on-one, seminar, role-playing, printed materials, and online. Study sponsors should identify common training requirements and develop effective methods appropriate to the topics and sponsor resources. For example, if a site monitor has experience recruiting subjects as a study coordinator, face-to-face training may be effective for that monitor, but online training may be more effective for sites with other monitors.

Numerous factors can prevent a site from implementing improvements. For example, the study coordinator may be enthusiastic, but not receive necessary support from the investigator. The investigator may be enthusiastic, but not be able to effect changes with the study coordinator. The site may have policies, procedures or internal politics that make improvements impossible. The site may be focused on bigger problems and higher priorities. The site monitor can diagnose such problems.

Study personnel typically have multiple conflicting priorities within clinical research and in other areas such as clinical care. Site monitors are very familiar with motivational methods such as encouragement, coaxing and threats. Additional methods will be discussed below.

Throwing advertising money at a shortfall in subject recruiting will probably not be effective unless (a) the cause of the shortfall is determined to be lack of advertising and (b) a specific

advertising program is likely to be effective. Site monitors can help sites develop effective advertising programs.

In allocating resources, the study sponsor should thus evaluate current site performance, its ability to help each site, and each site's ability and willingness to be helped. The allocation of each type of resources can then be prioritized. Each site should be evaluated individually so resources can be allocated for maximum effect. For example:

- If a site is unskilled at recruiting subjects and receptive to training, training is likely to be effective, but advertising dollars will be wasted until the training takes effect.
- If a site is unskilled at recruiting subjects, but does not want any advice from the sponsor, training will fall on deaf ears and advertising dollars will be wasted.
- If a site is skilled at recruiting subjects, but advertising is not an effective subject-recruiting tool for a specific study, advertising dollars will be wasted.
- If a site wants training in subject recruiting, but knows more about subject recruiting than the site monitor or other training resource, training will be wasted.
- If advertising will be effective, but the site cannot respond to inquiries in a timely manner, advertising dollars will be wasted. However, giving the site data on response time vs. enrollment may cause the site to fix the problem.

Adaptive Management

During site qualification and initiation, the study sponsor can assess site qualifications, attitudes and likely performance. Because information is limited, these assessments will be only approximate, so it will be difficult to allocate resources to one site and not another. The initial allocation is therefore likely to be relatively equal across sites.

As the study proceeds, the sponsor will learn more about site capabilities, attitudes and performance. With updated information, it can measure the productivity of the resources it previously allocated. For example, did the initial advertising budget generate enrolled subjects? Did the site welcome training? Did training in data entry improve data quality?

The sponsor can fine-tune resource allocations, retest, and continue sharpening the allocation over the course of the study. However, the allocation doesn't necessarily converge on the values that would have been established with perfect information at the beginning of the study. For example, one site may complete a competitive study and another may replace a skilled study coordinator with a novice. Resource allocations may thus shift between sites during the course of the study in unexpected directions. The sponsor may also decide to increase or decrease the total amount of a given resource in a study, or move resources between studies.

This process constitutes an adaptive approach to site management. Just as Bayesian statistics can be used to analyze safety and efficacy data, it can also be used to measure the impact of resource allocations and guide reallocations. However, statistical methods require data, which requires that the above measures be quantified. The impact of advertising dollars and subject recruitment training can be measured by the number of subjects enrolled. Training in data entry can be measured by the number of errors found by the site monitor and data managers. Site monitors can numerically score perceived receptivity to training and use a checklist to score implementation.

Adaptive methods require timely, analyzable data, so traditional non-quantitative monitoring reports filed according to traditional timelines, are not as useful as they could

be. A website for site monitors to enter pertinent data is better, and integration of data sources such as an automated randomization service is ideal.

Impact on Site Relations

Sites often complain that sponsors treat them as a commodity. It is demotivating to be treated as a commodity. This complaint is understandable when sponsors focus on treating sites consistently, rather than adjusting their approach based on what the site actually does. With adaptive site performance management, sites will perceive that they are not being treated as a commodity. Furthermore, if the sponsor explains cause-and-effect – and follows through – smart sites will modify their performance accordingly.

While it is generally unethical to reward sites with cash or merchandise bonuses for subject enrollment, rewards in training and advertising dollars are perfectly ethical. Imagine being a site monitor and telling a site the following:

“When we have worked with sites similar to yours in the past, we have found that the training we give in subject recruitment has yielded an average 30% increase in the rate of subject recruiting. Only half of these sites achieved their enrollment targets on that study. However, of sites that declined training, only 20% achieved their targets. Of sites that received the training, 60% conducted a subsequent study for us in the following year. Of sites that did not receive training, only 10% conducted a subsequent study in the following year. Would you like training?”

Increasing Precision

For more precise targeting of resources, more precise data is required. For example, site monitors could count the number of problems they find with informed consent forms and classify them by type of problem – missing signature, wrong version, etc. Each type of error could be numerically coded for analysis. As the study proceeds, it will become obvious which sites have which types of problems. It will also become apparent when multiple sites have the same problem, perhaps pointing to a deficiency in the protocol or case report form. A single site monitor may not see the pattern, but analysis of data from all sites will reveal it.

The same data will reveal differences between site monitors. Some site monitors will find more problems than others. One site monitor will find problems of one type, while another site monitor will find problems of another type. Study managers can use this data to identify site monitors who are especially good at one aspect of monitoring, and ask them to share their expertise with other site monitors. Caution is required in using this data because it may not mean what it appears to mean. For example, if a site monitor is not reporting a particular type of error, the site monitor may not be looking for that error, or may have trained the sites to not make the error.

With Bayesian statistics, data from one study can be combined with data from the next study. Over time, as site performance data is collected in multiple studies, a relatively stable picture will emerge of each site, each type of resource, each site monitor, etc. Trends will become apparent. For example, if a site reduces its data error rate over time, allocating training resources to that site is relatively likely to be productive. If a site's enrollment numbers correlate with advertising dollars, more advertising dollars are relatively likely to be productive.

Conclusion

Adaptation is nothing new to management practice; any good manager learns and adapts. Bayesian statistics and adaptive methods have now been proven on safety and efficacy data

in hundreds, if not thousands, of clinical trials. Perhaps it is time to apply this expertise to the business of managing research site performance.

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