

A predictive enrollment model answers critical questions in subject recruitment planning.

Removing the Mystique

Jill Pellegrino and Roger Smith

Any sponsor that has approached subject recruitment services with skepticism or trepidation can take comfort in knowing how we transformed over 10 years of patient enrollment data into a highly accurate predictive model.

Our predictive enrollment model answers two critical yet mysterious questions in recruitment planning: How many patients are we expected to get? And by when? The answers enable a trial manager to make a confident investment in recruitment. That is far preferable to the infamous black box “solution” that provides no performance expectations.

The Calculation

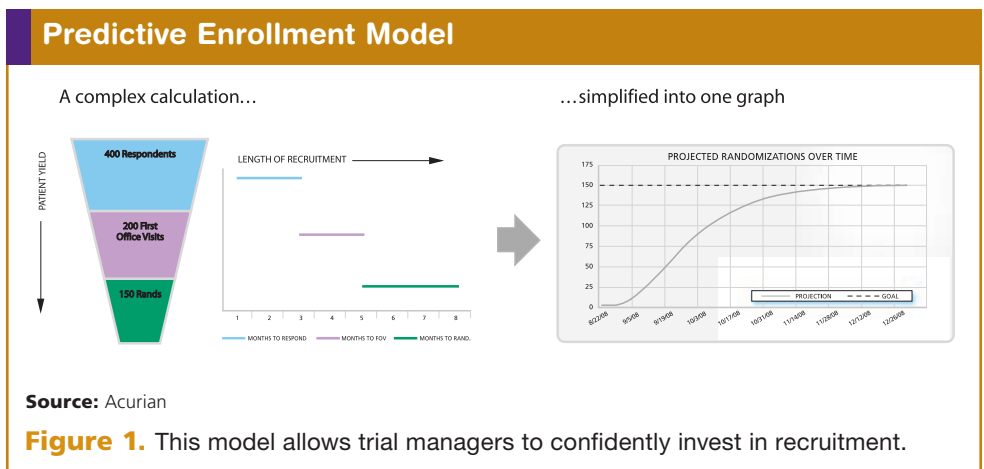
The model is based on calculating the interaction between the two principles central to predicting enrollment: protocol feasibility and recruitment stage timing.

Protocol feasibility is the probability that target patients exist in the addressable population and will agree to comply with clinical

and logistical protocol requirements. This is often expressed by a recruitment funnel. Recruitment stage timing is the average time for patients to complete each milestone in the recruitment process. That is predictable only by compiling an extensive database of recruitment performance history by therapeutic area (see Figure 1).

Patient yield. We all know that the number of respondents to a recruitment campaign does not equal the number of people who enroll in the trial. So the model projects the ratio of respondents to enrollees. The recruitment funnel is the input that governs the rate of attrition at every recruitment stage and ultimately determines how many patients enroll.

Estimating the recruitment funnel is difficult because no two trials are the same. A tiny difference between protocol requirements for two trials may cause drastic differences in achievability of recruitment and enrollment timing. This is why every protocol needs to be uniquely assessed. Unfortunately, most people use subjective



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methods to make estimates. Without having a scientific method to estimate patient yield, trial managers resort to anecdotes and guesswork to estimate the recruitment funnel, which rarely works.

Our recruitment performance database of over 1 million patients from actual trials enables an objective estimate of the probability that a patient will enroll.

The database shows exactly what percentage of migraine patients attend their first office visit, and how many Alzheimer's patients respond to a television ad or letter. The database enables the application of known probabilities to a protocol's requirements, defining the funnel with a high level of statistical confidence.

Recruitment length. The estimated number of enrolled subjects is only one piece of the puzzle. The other, equally critical, piece is the length of time it will take to recruit the required number of patients. Predicting enrollment timing also enables identification of unforeseen obstacles and

challenges early on. Solving problems early in the recruitment process is the key to successful enrollment completion.

Because timing is such an integral component of a predictive model, it is important to calculate it with confidence. Most recruitment models assume patients enroll in a linear fashion and that an equal number enroll per month. Using the database, which uses actual study data to measure timing behavior, we found that the timing equation does not follow a straight line but the behavior illustrated in Figure 2.

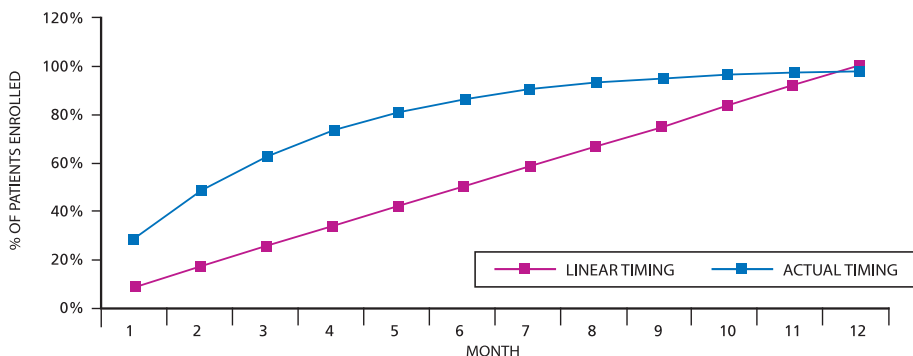
Expedited Enrollment

Traditional recruitment models use trend analysis to predict enrollment. On day one, a projection is created assuming an equal number of patients enroll each month.

As recruitment progresses, trial managers rely on matching the actual performance to the straight-line projection. When it diverges from that, they adjust the expected line accordingly. Adjusting projected expectations does nothing to help expedite enrollment, for two reasons. First, trend analysis relies on actual performance to make predictions. It takes time, sometimes months, before actual enrollment

Timing Assumptions

Actual Timing Used in Acurian's Predictive Enrollment Model

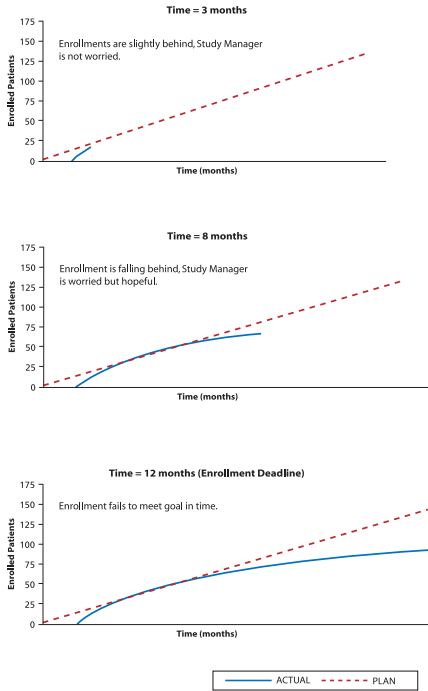


Source: Acurian

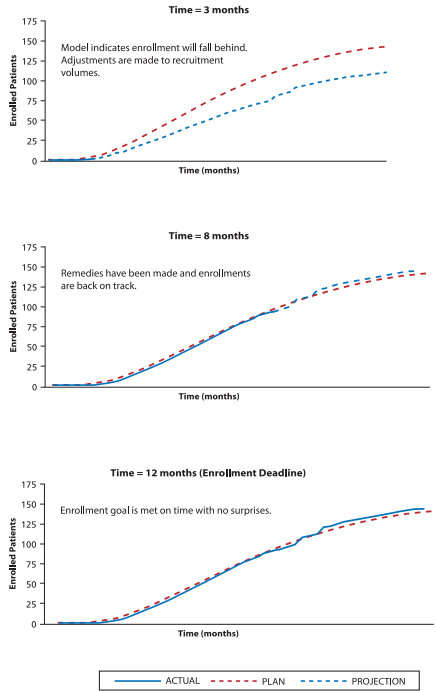
Figure 2. The recruitment model, which used data from over 400 actual trials, revealed that patients do not enroll in a linear fashion.

Comparison of Models Used to Complete Enrollment

Standard Trend Analysis



Acurian Enrollment Prediction Model



Source: Acurian

Figure 3. A side-by-side comparison of the two different recruitment prediction models over the same 12-month period.

performance is known. By the time the trial accrues enough randomizations to alert managers the plan is behind, it's too late to recover the original enrollment timeline.

Second, trend analysis is backed not by real performance but a flawed timing equation and a gut-based recruitment funnel. So the study team bases its recruitment plan on overly optimistic, impossible, estimations. Furthermore, spotting divergence from a projection provides no new intelligence to help finish successfully.

Contrary to trend analysis that reveals recruitment obstacles after they occur, predictive modeling identifies potential challenges up front, preventing them from transpiring. From the start, there is a realistic plan based on historical performance.

The predictive model projects the number of patients by day through each funnel

stage, not just randomization. This enables identification of harmful deviations that signify enrollment falloff before randomization. With this knowledge, recruitment tactic volumes are predicted to prevent an enrollment slowdown before jeopardizing the enrollment deadline (see Figure 3).

Investing in patient recruitment services does not have to be hit or miss. Predictability is not simply possible, it is measurably valuable to trial managers. When predictions are based on objective therapeutic data, they can enable study managers to design better budgets and build consistently attainable study timelines.

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