



Acurian on...

Patient Attrition in Clinical Trial Enrollment

Is There an Awareness Issue?

“Why does it seem so hard to recruit patients for a trial outside of my selected clinical site practices?” This is a question that Patient Recruitment Organizations (PROs) hear all the time from sponsors, particularly when it is increasingly difficult for the principal investigators (PIs) to source the majority of patients.

The challenges of recruiting and enrolling patients unknown to the research site are often a mystery to those who do not work in the space. The general expectation is that when a person is interested in a clinical trial and has the core disease, he or she will ultimately randomize into the study.

This paper examines the reality of the patient recruitment and enrollment process, what areas of attrition are the most challenging, how to address them, and what these points of attrition do to the overall cost of a randomized patient.

Generally speaking, the prevalence of trial awareness campaigns relative to the thousands of consumer marketing messages we receive in a day is miniscule. One could technically argue that there is a trial awareness issue overall, but it's not realistic to expect mass awareness for a very nuanced, fleeting “offer” like a geo-restricted, disease-specific clinical trial.

The good news is, such broad reach is unnecessary, as targeted marketing has gained significant traction and increased sophistication in recent years. This begs the next question: is the general public just not interested in clinical research? Contrary to many expectations, gaining interest from prospective participants is not the biggest challenge. When patients are initially messaged about clinical trials, they *are* responsive. This has been documented across all age, gender and race demographics in thousands of trials (see related Acurian paper on diversity).



Beyond Awareness and Interest

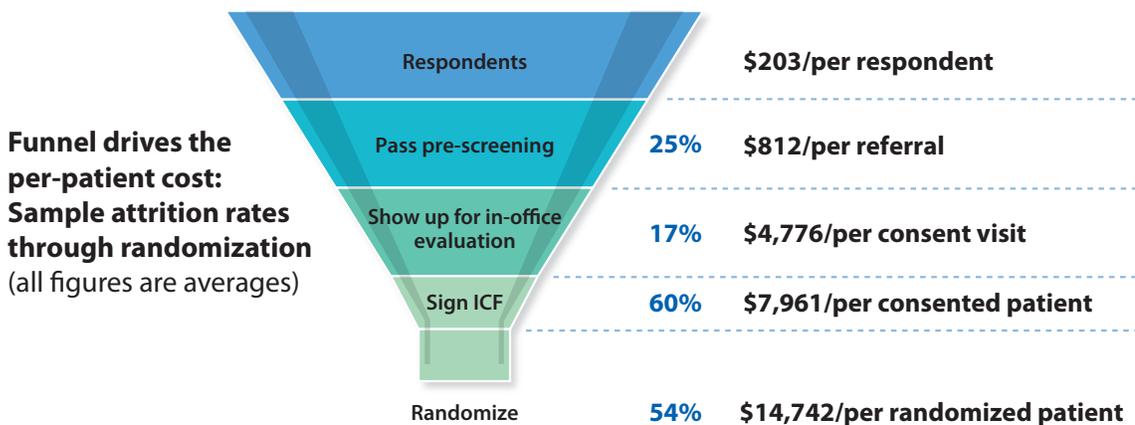
If the PRO has done its job well in targeting the right catchment area with an approved set of awareness materials, there should be a suitable response from potential study candidates. But creating awareness and interest is, as we have said, not the real issue. While it does take a reasonable investment to generate this interest and response, according to statistics compiled by CenterWatch.com (2014-15), getting patients from initial contact to randomization can be a difficult process. CenterWatch found that study volunteer attrition rates per enrollment phase typically trend as follows:

- 69% fail pre-screen
- 58% decline consent
- 32% fail screening

PROs often refer to this continuum as the “funnel.” However, this familiar industry metaphor is flawed, because the volume (of patients) entering the top of the funnel is far larger than the number that emerges (randomizes) at the bottom.

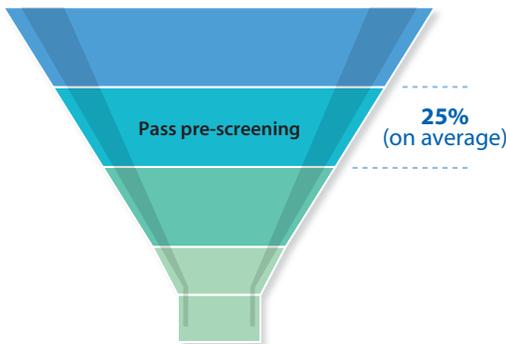
Across the many trials we have supported, Acurian has seen similar attrition point averages:

- 75-85% fail pre-screen
- 85% never show up to consent visit
- 50% decline consent
- 45% fail screening





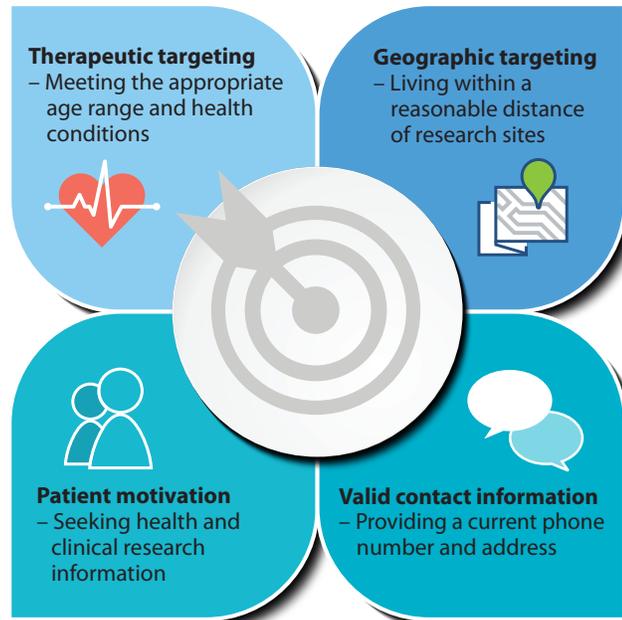
First Level: Pre-screening



Attrition at each level of the funnel is ultimately what drives the price per randomized patient. So, what are the factors influencing this attrition, and how can they be managed to lower the final per-patient cost?

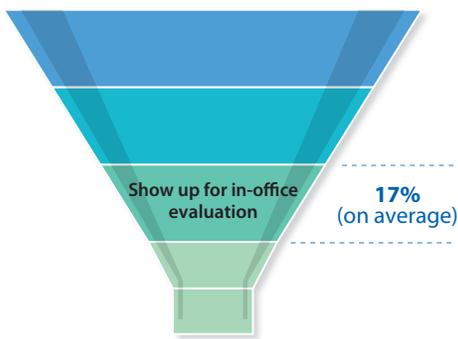
After their interest is attracted via marketing messages, potential trial participants may participate in pre-screening, either online or by contacting a call center. In either case, the pre-screening questions should be consistent, driven by the PRO's software and based on the trial protocol, to maintain proper referral quality.

Essentially, the PRO must act as gatekeeper, controlling the aperture of the funnel to filter out the majority of respondents who do not qualify, while capturing the remaining patients who self-report that they meet the necessary criteria for:





Second Level: First Office Visit (FOV, a.k.a. Consent Visit)



This level is primarily owned by the research site, as they are responsible for making a connection with each referred patient, scheduling the appointment, and walking them through the consent form. As the old expression goes, “You can lead a horse to water, but you can’t make him drink” – in other words, even after expressing interest and completing the pre-screener, many patients drop out of the funnel before ever making it to this first visit.

According to the National Center for Biotechnology Information (NCBI), “Patients who defer participation for a longer period are more likely to drop before completion. Longer time taken to complete the screening process increased the probability of attrition of all patients.”¹

The equitable recruitment of minority populations, women, and children for trials has become an important issue (see related Acurian paper). The NCBI concluded, “Compressing intervals between contacts is particularly important to retain minorities. One study found that the delays experienced in completion of screening were primarily due to inability of study personnel to contact patients.”²

Additional industry research suggests that 30 percent or more of patients referred to the site are typically *never processed or acted upon* by the site. Site personnel must be appropriately resourced to process the referrals to maximize the sponsor’s return on investment, ensuring the sites are committed to receiving the referrals and acting upon them in a timely fashion.³



The combination of site behaviors and patient behaviors is a wild card in the recruitment process, subject to many variable factors. In some cases, it's a matter of overcoming logistical issues (e.g., patients may have a difficult time getting to the trial location). Sometimes, it's more personal (e.g., patients must be motivated to go to a new doctor's office).

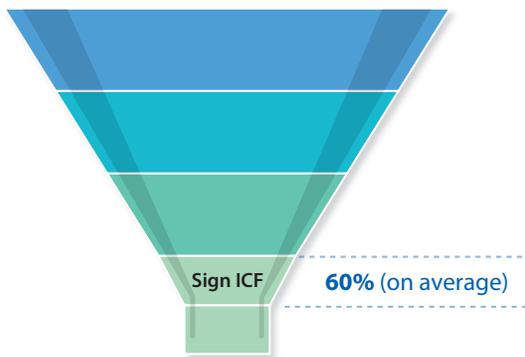
Common scenarios include:

- The site personnel may schedule the FOV too far out, and the patient's level of motivation deteriorates to the point that they are no longer interested in participating in the study.
- The site has no appointment reminder system in place to contact patients just prior to their scheduled office visit.
- Patients are mailed the informed consent form (ICF) prior to, or instead of, being scheduled for the FOV. The patient is left to interpret the information on the form themselves, which can be an intimidating and scary proposition.
- Patients may consult with their primary care physician or seek advice from family members, and as a result, be discouraged from participating.
- A poor customer experience when contacted by or when visiting the site can result in the patient having doubts and apprehensions about participating.

A participant's first impression of clinical research on this visit is critical to the entire trial, and patients must be able to ask questions and voice concerns. A two-way dialogue is integral to patient centricity (see related Acurian paper).



Third Level: Patient Consent



Communication during the consenting process can help ensure that patients stay enrolled in a particular study. If this aspect is confusing and difficult to comprehend, patients may not fully understand what they are going to be doing, leading to participants who will leave the study. A clear consenting process ensures that all newly enrolled patients completely understand all elements of the trial, increasing the likelihood of their completing it, because they won't be surprised by anything.⁴

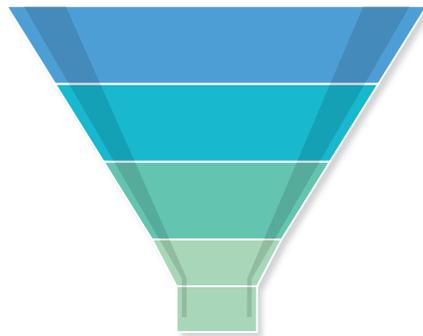
Practices that can positively impact the patient consent process:

- The principal investigator should be available to answer patient questions about the study, side effects, expectations, etc.
- The patient should be given time and a quiet place to review the ICF, with a pen and paper to write their questions and list concerns to be addressed by the PI or study coordinator (SC).
- The SC should allow adequate time for the patient to ask questions, making sure they have read and understand the ICF.

Patient objections to any part of the consent form can lead to additional attrition. They may be resistant to the number of visits or time commitment required for the trial, the types of testing or methods of treatment (e.g., injection or intravenous administration), the potential side effects, the level (or lack) of reimbursement, the need to wash off prior medications, or the possibility of receiving a placebo.



Fourth Level: Screen Fail



Randomize 54% (on average)

Once they have reviewed and signed the consent form confirming their decision to participate, each patient will be asked to share their medical history with the trial's principal investigator and submit to a physical evaluation (which may include lab tests or other medical procedures). Here is where attrition may occur that is based solely on the scientific and objective I/E criteria for the trial protocol.

In order to impact the screen fail rate, sponsors ideally should be looking at the patient recruitment strategy *at the same time* as they are writing the protocol. There needs to be greater emphasis on performing feasibility studies ahead of protocol design, as a reality check for the desired recruitment target. Too often, sponsors underestimate the rate of attrition at this stage, and end up making costly protocol amendments to randomize more consented patients who would otherwise fail the medical screen.



Conclusion

It is extremely important that the sponsor and PRO recognize the existence of these areas of attrition at the beginning of the trial, in order to set and document realistic expectations for the contribution the recruitment campaign will make to the overall enrollment goal. When all parties have a clear picture of where some of the bottlenecks or issues may lie, they can take more immediate and directed action to maximize the conversion of patients to ensure a successful outcome.⁵

Acurian brings efficiencies to different attrition points in the patient journey. This has significant implications for the per-patient cost. We work to minimize the cost at each level by proactively looking for potential problems before they start, and providing projected rates of attrition through our unique enrollment feasibility modeling. Even though we cannot control every factor along the continuum, we price at consent or randomization (the bottom of the funnel), because we can accurately predict how and when patient attrition will occur for the projects we propose to support.

¹ "Early Participant Attrition from Clinical Trials: Role of Trial Design and Logistics"
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2723836/>

² *Ibid.*

³ *Clinical Leader*, March 29, 2017

https://www.clinicalleader.com/doc/do-patient-recruitment-advertising-awareness-campaigns-really-work-0001?vm_tld=1993516&user=5287b1f6-1b44-4022-80f6-12665b005a2d&utm_source=et_6212879&utm_medium=email&utm_campaign=CLNCL_04-19-2017&utm_term=5287b1f6-1b44-4022-80f6-12665b005a2d&utm_content=Do+Patient+Recruitment+Advertising+And+Awareness+Campaigns+Really+Work%253f

⁴ Bio-Optronics blog: "Tips to improve your patient retention"
<http://bio-optronics.com/please-dont-go-6-tips-to-improve-patient-retention/>

⁵ *Clinical Leader*, above