Flipping the Funnel:

Strategies to Add Value to the Clinical Trial Patient Enrollment Process

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Summary

Despite advances in technology, and the onset of big data and social media tools, 80% of clinical trials are behind on their enrollment timeline.[1] After conducting thousands of clinical trials, WCG ThreeWire has observed specific critical points in clinical trial enrollment that can be optimized to reduce time and cost. Compared to the "spray and pray" methods of outreach that many companies use today, such as large-scale media campaigns, this systematic, yet adaptive, strategy can boost the number of qualified patients recruited, shorten recruitment periods and lower enrollment costs.

The patient recruitment process can be imagined as a funnel that channels patients into the trial and determines their suitability for the study. WCG ThreeWire advocates "Flipping the Funnel" by reprioritizing the usual patient recruitment strategies to draw in better-qualified candidates at the outset, while developing a strategy of community engagement that educates and empowers patients. To accomplish this approach, WCG ThreeWire recommends first reviewing a site's databases and electronic medical records to find known patients. The known patients—these are patients who already have an active, inactive, or prior relationship with the site, are much more likely to enroll and be retained throughout a study. Only after recruiting all eligible known patients is it strategic to advertise for new patients.

WCG ThreeWire's approach also focuses on recruitment and enrollment via the use of dedicated, trained Enrollment Assistants™ (EAs), who conduct a number of site-specific tasks related to patient recruitment, enrollment and retention. EAs not only offset the administrative burden of a site and conduct patient follow-up but can also engage other tasks such as appointment scheduling, transportation, data entry and more. EAs follow patients through a rigorous program of "high tech—high touch" communications, which fosters informative interactions with patients throughout the clinical trial process. As the EAs connect with trial participants throughout multiple human touchpoints, from initial recruitment planning to consent, they foster stronger relationships with patients, which can result in improved retention. One case study of a WCG ThreeWire EA-supported site showed a 500% increase in patient enrollment rate compared to a similar site enrolled by conventional methods.

Introduction

Why Eliminating Bottlenecks in Patient Recruitment Cuts the Costs of Clinical Trials

- **Clinical trials are expensive.** Bringing a drug to approval can cost an average of $1.4 billion [in 2013 dollars], according to a 2016 Health Economics study.[2] One meta-analysis estimated that a single study, depending on size, can cost from $40 million to over $100 million to conduct, and that a randomized clinical trial can cost from $43,000–$103,000 to $254,000 per patient.[3]

- **Trials are more complex,** and they increasingly focus on rare diseases and use of personalized medicine that target sub-populations of patients. Between 2001-2005 and 2011-2015, the number of clinical trial endpoints rose by 86%.[4]

- **Trials are longer.** The average duration from site identification to study start-up completion is now 31.4 weeks, one month longer than the average duration observed 10 years ago.[5]

Barriers such as difficulty in recruiting and retaining participants, lack of a trained clinical research workforce, issues with sponsors, regulatory and administrative hurdles, and poor coordination between clinical research and medical care can increase costs and delays.[6] A 2015 analysis of registered trials revealed that 19% were closed or terminated early because they could not accrue enough participants. As much as 86% of clinical trials do not reach recruitment targets within specified periods. According to the Clinical Trials Transformation Initiative (CITI) Task Force, simply improving recruitment planning could increase the quality and efficiency of clinical trials.[7]

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How to Remove Trial Bottlenecks

According to Kunal Sampat, founder of the Clinical Trial Podcast, a podcast for clinical research professionals, from the sponsor's perspective, top bottlenecks in clinical trials include protocol design, site selection, staff distraction and overload.

- "When a clinical protocol is written by an academic rather than a physician or clinician, it may seem as if it contains ideal criteria, but the real-world challenges of enrollment can be very different," says Sampat. "While this will allow them to get a protocol or the actual data approved by the FDA and then finally get their product on the market, you have to **get input** from your clinicians when you're designing a protocol."

- While clinical trial sites are often selected because of the prestige of the institution or researcher, Sampat estimates that only 20% of sites actually contribute to enrollment. He recommends selecting sites by their patient enrollment potential. "At the end of the day, you have to **look at the data** in the patient electronic medical records of a center or research department, and pull that data out to see if it matches the protocol," Sampat says.

- **Minimize staff distractions** inherent in managing multiple trials. "There's so much information that site staff has to absorb and usually the site isn't staffed to the level of sponsor facilities," says Sampat.

Further Recommendations to Remove Bottlenecks

Sampat also recommends:

- Ensuring that the research coordinator is trained in good clinical practice—but avoid repetitive trainings.
- Eliminating training gaps by shortening the duration between initial training with the hospital or research department and site enrollment.
- Communicating realistic enrollment goals to internal teams and external site CROs.
- Making referencing enrollment criteria easy with pocket cards for quick reminders.
- Fostering interactive communication with sites by regular conference calls or webinars instead of newsletters.
- Following up with patients promptly.

Bottlenecks in the Patient Enrollment Funnel Can Add to Trial Cost

Studies can experience enrollment delays because they lack enough qualified patients, and/or because the site can't promptly and effectively process patients and follow up with them.

According to Seth Nelson, WCG ThreeWire vice president of operations, enrollment and retention issues must be addressed in tandem because they are a bottleneck leading to patient attrition. Not having enough qualified patients can extend the study enrollment period, require more resources and may even lead to the poaching of patients from other trials. Excessive patient attrition wastes limited resources and can be a red flag that patients are insufficiently qualified at the outset.

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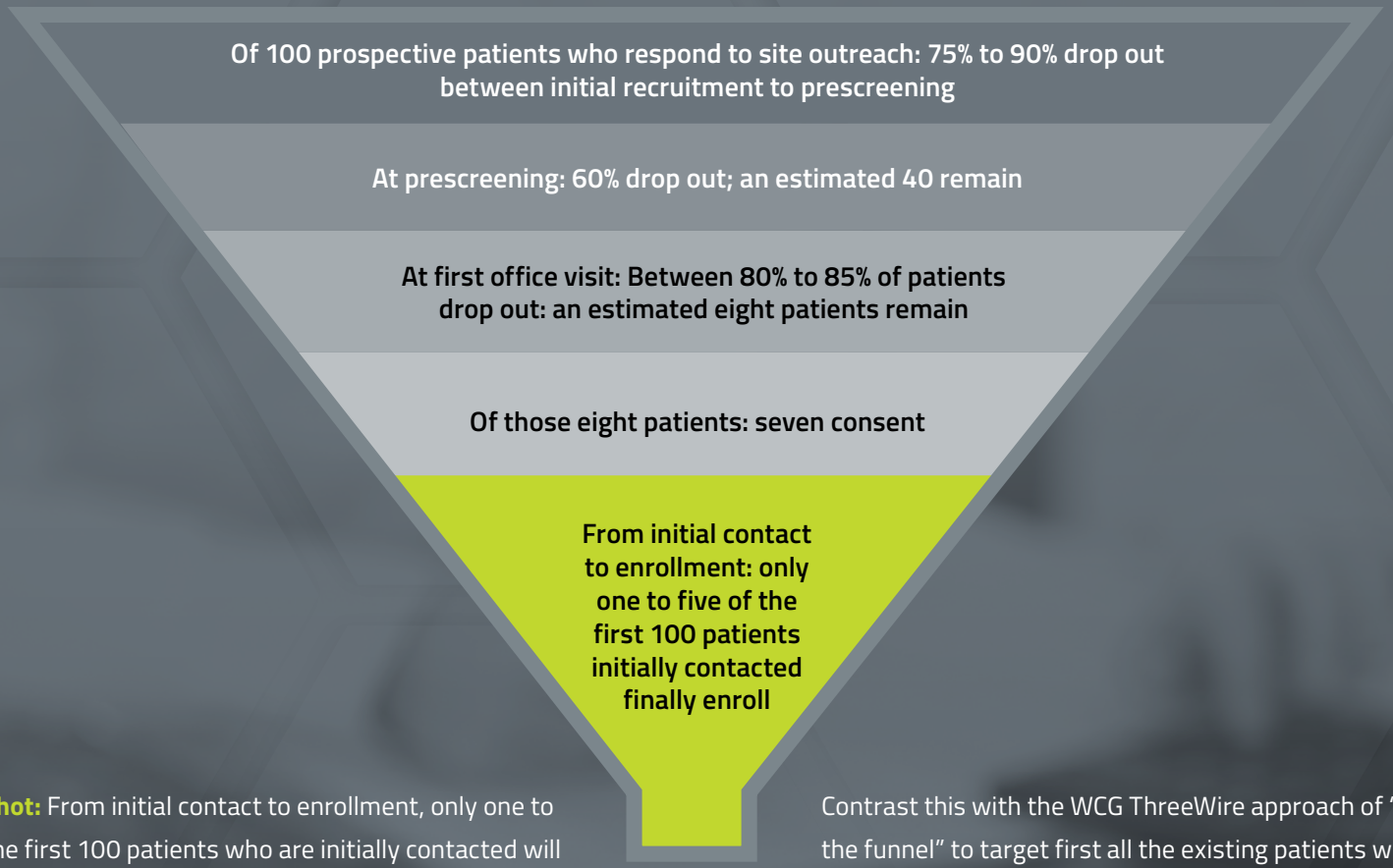
The Patient Enrollment Funnel:
What it Takes to get 100 Patients to Consent to a Clinical Trial



The upshot: From initial contact to enrollment, only one to five of the first 100 patients who are initially contacted will actually enroll in a study. This is partly due to the common strategy of first recruiting unknown patients to the site.

Contrast this with the WCG ThreeWire approach of "Flipping the funnel" to target first all the existing patients who are known to a site by mining databases and electronic medical records and then to reach out to recruit unknown patients.

Why Flipping the Funnel Works

WCG ThreeWire estimates that it costs between $10,000 to $20,000 to recruit a patient, depending on the therapeutic area. As 75% to 90% of patients drop out of a clinical trial between the initial referral to their first office visit, optimizing the trial enrollment process can make a difference. If the patient recruitment process is imagined as a funnel where patients' suitability for the study is determined, "Flipping the Funnel" can shorten trial enrollment time by two to three months. "We typically see cost savings of about 50% per patient enrolled, so your return on investment is significant," says Nelson. "If you can be first to market, the money and market share you can capture will show the full potential return on investment of decreased study timelines."

WCG ThreeWire recommends an initial patient recruitment strategy prioritizing finding patients known to the site first, by using systematic Chart Review™ or database mining. These patients will be the most cost-effective and invested in the study. Once the supply of patients known to the site is exhausted, using other tactics such as community outreach, social media and traditional media to recruit new patients will be effective.

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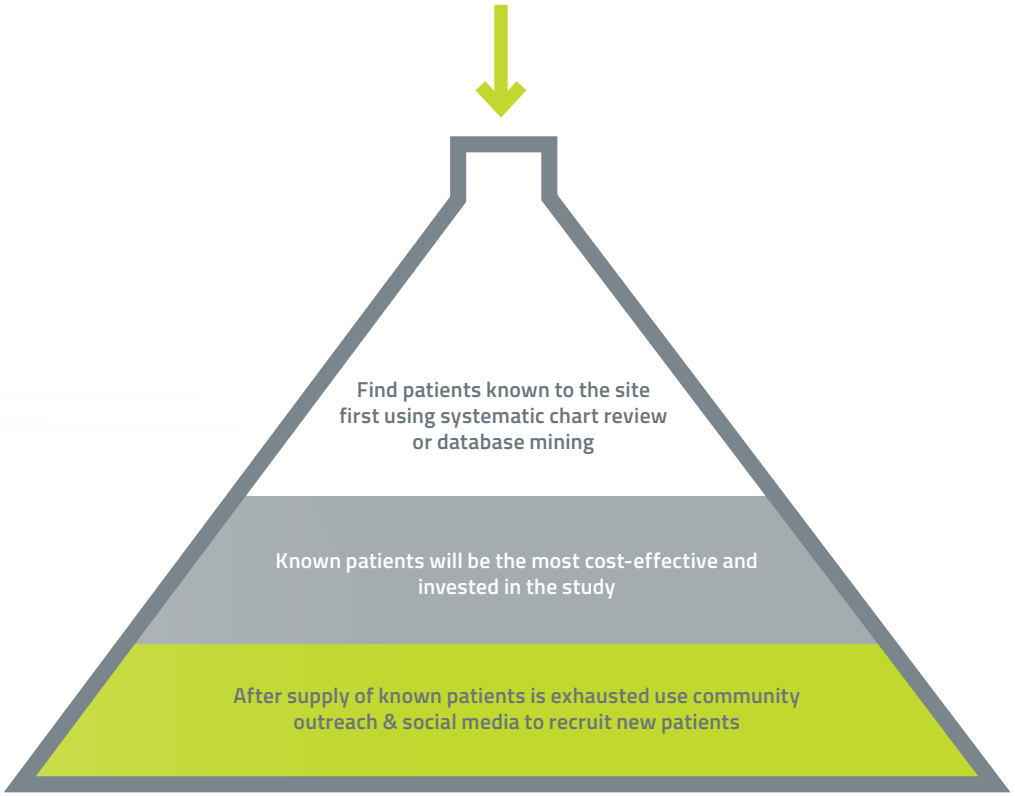

Uncovering the Hidden Bottlenecks in Patient Recruitment

How finding known patients is supposed to work: Finding patients known to the site already is typically accomplished by conducting a database or Chart Review.

What happens in reality: Lack of coordination and follow-up on patient outreach can occur. The study sponsor typically assumes that they will acquire a certain number of patients from every site. But when the site gets busy, staff are unable to spend time reviewing the charts and contacting those patients. The study coordinator's attention may be divided between several different studies.

"If the study coordinators get a stack of 30 or 40 other individuals to screen for a given study, and they have five to seven other studies that they are managing, they don't have the time to spend 15 minutes on the phone screening potential volunteers, so the follow up doesn't happen," says Nelson. This can also lead to poor initial vetting of candidates and make it difficult to track resources expended, particularly in the case of multiple clinical trials, raising the risk that eligible patients may be poached from other trials.

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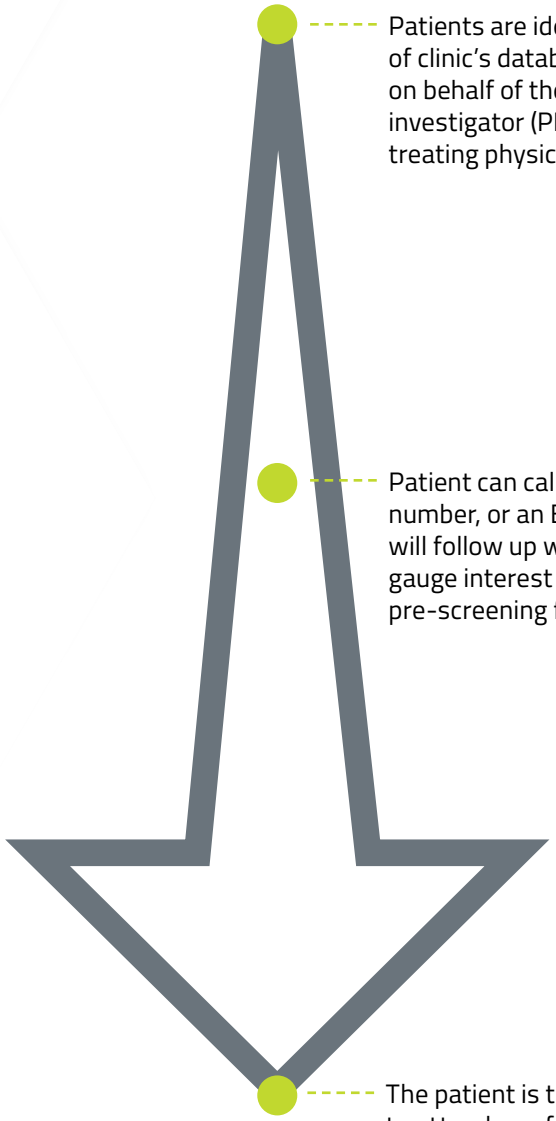
Seth Nelson, WCG ThreeWire vice president of operations

How WCG ThreeWire Manages a Systematic End-to-End Database Review

Patients are identified from the review of a clinic's database and sent a letter on behalf of the physician principal investigator (PI), who may be their treating physician. The patient can call a dedicated study number, or an Enrollment Assistant who will follow up with the patient to gauge interest and complete a full pre-screening for the study. The patient is then scheduled to attend an office visit to consent for the study.



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Key Points to Remember

Each site needs its own specific recruitment plan.
Scheduling between patients, caregivers, PIs and sites must be coordinated, as well as maintaining communication and attentive follow-up. Moreover, PIs often balance research with clinical practices, so it can be challenging to coordinate their schedules with those of the site.

It is critical to understand the prospective patient's needs.
In a women's health study, for instance, participants can be middle-aged mothers with multiple responsibilities. And patients cannot be considered in isolation. "For example, in an Alzheimer's disease study, you are not recruiting just the patient, you are recruiting the caregiver," says Nelson. "In oncology, the individual typically has a care team that has conversations and decides on the direction of care [together]."

How "Flipping the Funnel" in Patient Recruitment Can Prevent Attrition Later

WCG ThreeWire focuses on the specific window of patient enrollment between the study initiation visit (SIV) after the study sponsor "greenlights" patient recruitment to consent. This is because any subsequent bottlenecks after patient consent are generally due to the protocol and are not site-specific. Here are some tactics that WCG ThreeWire recommends to keep trials on track:

- **Adhere to a specific schedule for patient contact**
  Conducting the Chart Review and media outreach from initial meeting to startup can take three to six weeks from program initiation to patient recruitment. If a patient expresses interest in a trial as a result of a media campaign, he or she should be contacted for a prescreening call within 24 hours and scheduled for an on-site visit five to seven business days after the initial contact. Using a trained EA to follow up with patients provides an essential human touch and ensures that nobody falls through the cracks. WCG ThreeWire assigns trained EAs to study sites to follow patients until they give consent, as well as to develop crucial relationships with patients and listen to their concerns. "No matter what trial we are running, those patients, their lives are interrupted," says Nelson. "They want to feel that they are cared about and are part of something."

- **Relieve the site coordinator of work**

  "Site coordinators can talk to hundreds of patients for a single study," says Nelson. "And when you have six, eight, 10 studies you are following up on, regular patient communication doesn't just happen. We make sure the follow-up happens with a dedicated and qualified individual to that study. The EA will also assist with appointment scheduling, reminder calls, scheduling transportation for patients and data entry. The dedicated EA creates a perfect-world scenario for the site. That is where the results come from."

- **Consult with the PI and site coordinator on the desired trial workflow**

  "This extra layer of communication aids in determining how to schedule resources to address site needs and the appropriate metrics by which to measure the study progress."

> **"The dedicated EA creates a perfect-world scenario for the site. That is where the results come from."**
>
> **Seth Nelson,** WCG ThreeWire vice president of operations

Every Patient is Important, but Known Patients Should be Prioritized

WCG ThreeWire follows up on all known patients within a site's internal network first. These patients are the most economical to acquire, as the site already has information about them. Because they are most familiar with the site and are most comfortable with the care that they get there, they are usually the quickest to recruit and most compliant patients on the study. "We focus there first to be sure that the drop-off is limited," says Nelson.

WCG ThreeWire can conduct a Chart Review or mine the internal databases of a healthcare institution before a site is activated. This method enables developing a patient list and a deeper pool for recruitment once a site is active. "We prescreen them further, reach out to them to provide a personal touch and that makes the difference," says Nelson. "This is because the patient and the EA has through this process built up a relationship similar to the one the patient has with the doctor's office or investigator."

Only after the supply of known patients has been exhausted, will WCG ThreeWire reach out to unknown patients with a wide assortment of strategies that include physician referral networking, community outreach and media campaigns via various media channels (online, advertising, banner ads, etc.). This helps limit delays in care.

Rescuing Trials From Bottlenecks After Enrollment Has Started

In an alternative scenario, where a trial must be rescued because a site has run through known patients and has hit a bottleneck, it is necessary to locate and reach out to unknown patients to get the recruitment process back on track.

Conclusion

Flipping the Funnel Adds Outsized Value

A strategy that focuses on boosting the percentage of patients that come through the top down to the bottom of the funnel will have a much more significant, more positive impact than trying to make up for lost time in populating a site. “Flipping the funnel and applying the right resources at the right time can keep sites enrolling,” says Nelson.

ABOUT WCG THREEWIRE

Since 1999, WCG ThreeWire, a leader in clinical trial recruitment and direct-to-patient marketing, has been helping pharmaceutical, medical device and biotech companies achieve their patient recruitment, enrollment and retention goals.

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Sources

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