

Technology Enhanced Patient Recruitment: A Community Approach

What if you ran a clinical trial and nobody came? Inadequate planning for patient recruitment costs time and money; but targeting the right people the right way will keep trial numbers high.

Despite the growing trend to accelerate clinical research, the US Food and Drug Administration (FDA) says that the drug development path is becoming increasingly challenging, inefficient and costly.¹ Process improvement initiatives have been implemented and revisited by many pharmaceutical companies, with the aim to make internal processes more efficient and to speed up clinical development. However, one of the steps in any clinical trial that remains out of the direct control of the sponsor is patient recruitment — companies rely upon the promise of investigators to achieve their required study numbers.

Researchers managing clinical trials will cite patient recruitment as their single most difficult barrier to meeting study timelines. Centerwatch reports that 45% of study delays are because of slow patient recruitment and that, on average, most delays exceed 6 months.² According to a 2002 white paper from IBM, 80% of studies fail to meet their recruitment timelines.³ Despite the pre-study promise of patients, an estimated 30% of study sites fail to recruit a single subject.⁴ This problem is likely to worsen as the number of clinical trials continues to increase each year and many drugs become more focussed, therefore targeting smaller patient pools. This bottleneck in the study recruitment period is symptomatic of a deeper problem.

The real problem is that despite their focus on process improvement and acceleration, many pharmaceutical companies are failing to take a proactive approach to patient recruitment. In fact, the majority of trials are set up for failure: action is not taken until they are unable to recruit and timelines become unacceptable. In such situations, sponsors contract the services of patient recruitment firms to perform a rescue. Conventionally, these can involve large sums of money for media campaigns; they require urgent implementation, time and — in particular — the ethical approval process, which may limit the tactics that can be practically employed in a short time frame. Such limitations may affect the ability of a campaign to effectively and efficiently deliver the desired results.

Rescue mode absorbs resources that would otherwise be applied to forthcoming trials, meaning that additional

unplanned delays in the overall development plan are possible. The main problem, therefore, is that many companies do not plan ahead effectively, or make budgets available, for patient recruitment — short-sightedly relying upon site estimates of patient numbers despite the evidence of previous experience.

However, trends indicate that a break in this cycle is imminent. Many clinical development departments have observed these shortcomings and are beginning to learn lessons from their marketing departments. New specialized patient recruitment departments that act as consultants to their drug development programmes are gathering a toolset for patient recruitment, comprising a whole suite of solutions — a subset of which may be applicable to enhance recruitment for individual clinical trials. Their aim is to both accelerate patient recruitment and make this step in the process more predictable and reliable.

Patient recruitment solutions

The most common proactive approach to expanding the pool of potential patients (beyond those known to the clinic) involves media campaigns. Adverts for clinical trial participants are placed in a variety of media including local and national newspapers, lifestyle magazines, local radio, clinic leaflets and posters. They may even engage the involvement of community outreach organizations and sometimes include television advertising (although this is rarely employed outside of the US). Interested candidates are directed to a telephone number and/or website where they can learn more about the study and answer simple questions to determine their qualification for a formal screening visit. Telephone screening can be successfully performed by staff at individual study sites, call centres and using interactive voice response (IVR) systems.

Many pharmaceutical companies have the perception that this style of advertising is unethical or prohibited in numerous countries outside the US, but in fact it is acceptable to both ethics committees and regulators in most countries — although there is much variation in the nature and form of advertising deemed appropriate. The EU Clinical Trials Directive⁵ states that

Bill Byrom*

is product development director at ClinPhone Group Ltd, Lady Bay House, Meadow Grove, Nottingham NG2 3HF, UK. Tel. +44 115 955 7333 Fax +44 115 955 7555 info@clinphone.com

David Stein

is director of strategic business development at ClinPhone, Inc., Princeton, New Jersey, USA.

Regan Carey

is senior project director at NCERx, San Diego, California, USA.

*To whom all correspondence should be addressed

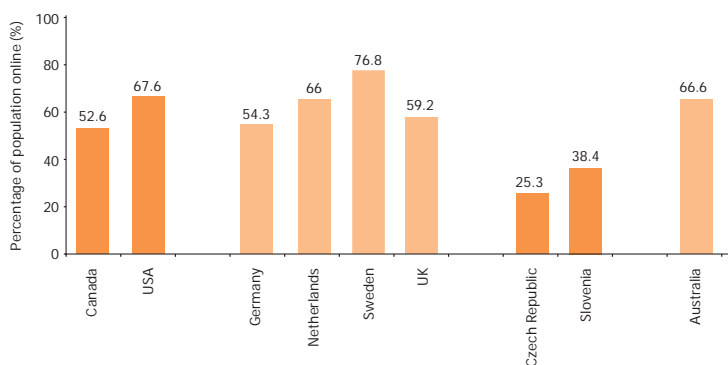
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recruitment by advertising is permitted in member states and outlines requirements for ethical approval of such approaches.⁶ Such use of media has the potential to reach large populations simultaneously; however, there are usually high costs associated with adverts and their “shelf-life” is very short. Details of this style of patient recruitment are well documented elsewhere, and is outside of the scope of this article.

Outreach via the Internet

Internet use is rapidly expanding. Recent data sourced from Nielsen Net Ratings (NNR) and the International Telecommunication Union (ITU) estimate that 66.1% of the population in North America and 28.1% across the whole of Europe have access to and use the web (Figure 1). NNR estimates for January 2004 indicate that 67.6% and 52.6% of the population are online in the US and Canada, respectively. Figures for Western European countries include: 76.8%, 66.0%, 59.2%, 54.3% for Sweden, The Netherlands, the UK and Germany;⁷ with web usage in Eastern European countries rapidly catching up: for example 38.4% and 25.3% in Slovenia and the Czech Republic, respectively.⁸ In Australia an estimated 66.6% of the population use the Internet.⁷ A recent study of 2204 adults conducted by Princeton Survey Research Associates reported that 66% of Internet users older than 65 years have searched for

Figure 1: National web usage statistics.^{7,8}



health or medical information online, the majority of searches relating to information about a specific disease, medical problem or treatment.⁹ This is equivalent to the percentage of the general Internet population searching for such health care information. The Internet, therefore, represents an expanding community and has great potential for enhancing patient recruitment into clinical trials if applied effectively.

Community-driven approach

Early approaches at patient recruitment using the Internet yielded disappointing results. There are billions of websites worldwide; this fact alone can limit the ability of web users to locate a relevant clinical trial opportunity. Banner advertising and pop-up messages irritate web users rather than present them with information of relevance — these are generally ineffective methods of directing traffic to a clinical trial opportunity. Moreover, this approach is limited to the subset of patients who are actively seeking a clinical trial and ignores those who may

be interested if presented with relevant information.

Many web users will seek information about medical conditions and treatments from time to time. Beyond the small subset who actively search for a clinical trial opportunity, the larger pool of users represents the target population for a therapy under investigation, and specifically for a particular clinical trial. Combining relevant, accurate and impartial health care information with education and information about clinical trials in general, and specific clinical trial opportunities, online communities can engage their audience with regularly updated information and communications — enabling long-term relationships to be built that enhance the lifestyle of the subject. Through such communities, effective education and information about clinical trial opportunities can be delivered, providing a highly targeted and effective way of reaching out to the target patient population.

The recruitment pool for clinical trial candidates is, after all, a subset of the total market for the therapy under development. Indeed, the only differentiators between the population targeted by the therapy and the recruitment subset are (a) a potential patient’s knowledge of the clinical trial opportunity and (b) their willingness to sign an informed consent to participate. By developing and using online communities of patients, this facilitates — in an efficient and focussed way — the widening of the pool of target patients who have knowledge of the clinical trial opportunity; and, through education, may increase their willingness to be a part of such activities.

Practical application of community-driven web approaches

The typical Internet user visiting medical and health care sites approaches the web seeking answers to questions and solutions to problems. They don’t want intrusive advertising, cookies cluttering their hard drive or complex site navigation. **Simple information-rich clustered sites.** To maximize the opportunity of presenting clinical trial opportunities, health care websites must attract a high number of regular visitors. To do so, they must deliver high quality content to tightly defined audiences. Information design can be used to provide answers in an easily scanned and understood format. Diagrams, illustrations and charts address the needs of a variety of readers. Multiple sites allow access to different aspects and health care questions; multiple reading levels can be catered for so that subsets of the populations are not excluded from effective access to information.

Linking these sites into a cluster, each with familiar style and branding, provides a wide library of resources to the visitor focussing on symptoms, treatments, general information about a condition, lifestyle implications, new treatments in research and clinical trials. Links can be established between clusters so that the user can easily navigate to sites containing information on related conditions and interest areas. For example, a site relating to diabetes care and treatment may also contain links to information sites about erectile dysfunction, obesity, hypertension, diet and health and other related topics.

Navigation design. Effective use of links between pages and sites can be established using a technique called foreshadowing that clearly explains to the user why they should click on a certain link and the expected content of the destination page. For example, links can simply indicate the content of the destination page ([Learn more about clinical trials](#)), or indicate that an action is forthcoming ([Click here to register](#)). Complex destination pages benefit from relatively

detailed foreshadowing. For example:

An initial medical screening asks you a series of questions about your health and your medical history. The information is completely confidential.

[Click here to begin your online medical screening.](#)

This ensures that visitors do not find themselves travelling up many cul-de-sacs in their search for the information they require. Dead ends create impatience rather than engagement and cause visitors to leave the site and abandon their search. Foreshadowing typically increases user response by 350%.¹⁰

Links can also be created dynamically based upon the visitor's psychographic profile. The sites that a user has visited in a single visit can be tracked. Compared with the path and actions taken by previous visitors, it is possible to anticipate the information and destination site likely to be sought by an individual visitor. Links to websites considered of most interest can then be dynamically presented for the user to rapidly and efficiently navigate to the information required. Psychographic methods can also determine which hard links should be established between websites to facilitate navigation. This is valuable to the users of the web network and increases their engagement and trust.

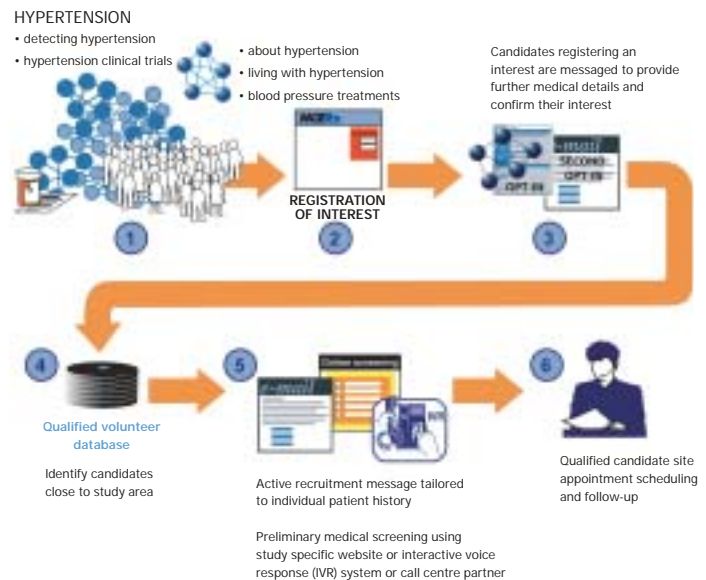
Building engagement and trust. Although privacy is one of the major concerns of the Internet user, particularly those using health care websites, information fulfilment is the key attraction for the majority of site visitors. Well designed and implemented surveys, screens and polls engage the user, and effective long-term relationships that are built through permission-based communications enhance the lifestyle of the user. One way to achieve such relationships is by allowing site visitors to register to receive regular information, updates and newsletters that are delivered in a reliable manner and contain information that is relevant and interesting. Sites and clusters develop a large volume of regular, engaged visitors, some of which also indicate an interest in clinical trials relating to their condition.

Building a clinical trials candidate database and recruiting subjects. A community-based web network can be used to enrol and prescreen potential study candidates (Figure 2). Candidates visiting the network of websites to access valuable health care information can also find general information about clinical trials and new treatments (Step 1). At any site, visitors can 'opt-in' to register an interest in finding out more about clinical trials, without any commitment (Step 2). Once opted-in, registrants will immediately receive an e-mail thanking them for their interest and requesting more medical details to match them to current and forthcoming clinical trial opportunities (Step 3). This stage requires their permission a second time and reconfirms their interest in receiving information regarding clinical trial opportunities. In effect, this second step requires their second opt-in.

Messages direct candidates to a generic screening website requesting basic medical information along with their geography. This creates a database of potential candidates with a variety of medical conditions and demographics. Continued traffic through the cluster of sites ensures the continued growth of the database. Databases constructed in this way are only of value if they are current. By messaging database candidates on a regular basis, their continued interest and relevancy is ensured. Those candidates failing to maintain an interest should be withdrawn from the opted-in database.

It is important that databases maintained in this way comply with relevant data protection and Health Insurance Portability and Accountability Act (HIPAA) regulations. Patient

Figure 2: Development and use of a clinical trials candidates database.



information should be separated from identifiable data. These can be linked, for example, using independently held encrypted keys. In addition, messaging of subjects can only be performed with the specific permission of the subject.

When a new clinical trial opportunity arises, the database can be interrogated to identify candidates meeting the basic study requirements and located within a defined radius of the predefined study sites (Step 4). Identified candidates can be messaged by e-mail, informing them of the forthcoming study and inviting them to complete a study prescreening questionnaire either by telephone or via the web (Step 5). The content of these messages is subject to ethical approval. Because messages are sent only to relevant candidates, and because the database contains double-opted-in subjects (that is, those that have registered an interest in participating in a study on

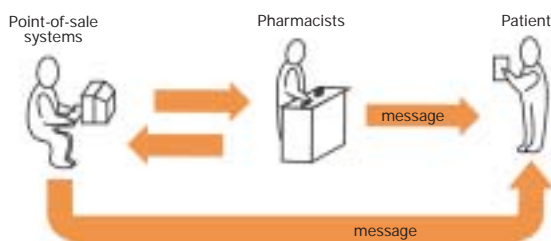
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two successive occasions), the response rate is likely to be relatively high compared with other approaches. Finally, formal site screening appointments can be arranged for those deemed qualified by the prescreening process (Step 6). This process boosts initial site recruitment activities and provides a continual feed of new candidates throughout the recruitment period.

Other technology approaches

As discussed above, the target population for a clinical trial generally represents the population targeted to receive the marketed treatment. In addition to the Internet pool of health care information seekers, the clinic pool of patients can be extended by considering those currently receiving prescriptions relevant to the diagnosed condition. Many pharmacies in various

Figure 3: Point-of-prescription messaging and recruitment.



countries use centrally controlled software and database applications to administer the prescription process and manage reimbursement activities. Such central databases contain a rich source of data, often supplied to pharmaceutical sales organizations in aggregated form to assess prescribing behaviour in their different territories, and hence direct the attention and tactics of the sales force.

Such software systems also present an opportunity to effectively message a patient at the point of prescription. Based on the age, sex and current prescription of a pharmacy visitor, it is possible to determine whether they might be suitable to be considered for a clinical trial opportunity. In this case, prescribing software within registered pharmacies can direct the messaging of that patient in a variety of ways (Figure 3). For example, messages may take the form of information leaflets printed at the pharmacy to be included with the prescription; tagged medication labels on which the removable tag contains an additional message (Figure 4); or a verbal message delivered by the pharmacist.

Figure 4: Patient messaging via prescription labels.



These messages may be an invitation to find out more about a specific clinical trial operating locally. In this case interested patients will be directed to a website or toll-free telephone number to find out more about the study, and determine whether they would be qualified to attend a clinic screening assessment. Alternatively, these messages may direct patients to information about their condition presented over the Internet. In this way they may visit a health care information cluster, become engaged with the material and learn more about clinical trials in general. This increased traffic to the disease-specific websites can lead to significant increases in the size of the opted-in candidate database for that condition.

Discussion

Patient recruitment activities beyond clinic referral rarely involve a single tactical solution, and will most likely be composed of a variety of approaches including technology and conventional media solutions. Previously, the Internet has had mixed results in patient recruitment, mainly because of the methods used to direct traffic to recruitment opportunities. Investment in informing and educating the patient popu-

lation results in the development of a loyal, engaged and growing online community that utilizes and benefits from the health care information resources and communications provided. Having accessed educational material regarding clinical research, a proportion of these patients will register to be contacted about forthcoming trials. Databases generated in this way provide a very measurable approach to assessing the potential returns of web recruitment. Upfront it is known how many candidates satisfying the study criteria and located close to a study site can be contacted immediately. These direct communications are more focussed than any other patient recruitment approach — they are only issued to subjects suffering from the specific condition of interest, and subjects who have already expressed an interest in participating in a clinical trial — making such an approach attractive and low-risk.

In addition to the existing candidate database, many more potential subjects are likely to register an interest through the site cluster when an actual clinical trial opportunity is presented. It is also possible to greatly increase traffic to a site/cluster whilst actively recruiting an individual trial by modifying the interlinks between sites and using affiliate feed via links from marginally related websites, and additional public relations such as published adverts or drug label messages.

A database of opted-in candidates also has great value during the planning stage of a clinical trial. Hot spots representing high numbers of candidates can be used to select optimal site locations, and thus maximize the potential of recruiting patients using this approach. Direct messaging of patients at their point of prescription provides a second powerful technology solution. Again, this provides increased focus compared with other more conventional forms of advertising.

Appropriate use of technology has great promise in enhancing patient recruitment. Pharmaceutical companies are becoming better prepared to include additional patient recruitment activities as part of their pre-study planning and budgeting. Using technologies in the ways discussed here provides cost-effective and focussed approaches that are valuable components of the patient recruitment toolkit.

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