

Meeting Patient Recruitment Timelines

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As pharmaceutical and biotechnology companies increasingly focus on optimising the return on each dollar, pound or euro invested in R&D, clinical trials are coming under intensive scrutiny. Certainly, there is considerable room for improvement in clinical trial performance: for example, some 80 per cent of clinical studies take longer than expected. Every extra day a drug spends languishing in development potentially costs the sponsor at least US\$600,000 in lost sales. Indeed, lost sales could reach US\$8 million for each day a potential blockbuster is delayed (1). More immediately, keeping a trial running costs around US\$40,000 a day.

As a result, sponsors and clinical research organisations (CROs) now scrutinise the details of every step in clinical trials – from protocol development to supply logistics, to data capture – to ensure that drugs reach the market with as little delay as possible. Patient recruitment and retention emerge from such analyses as among the most critical steps in determining whether a study is completed on time and on budget.

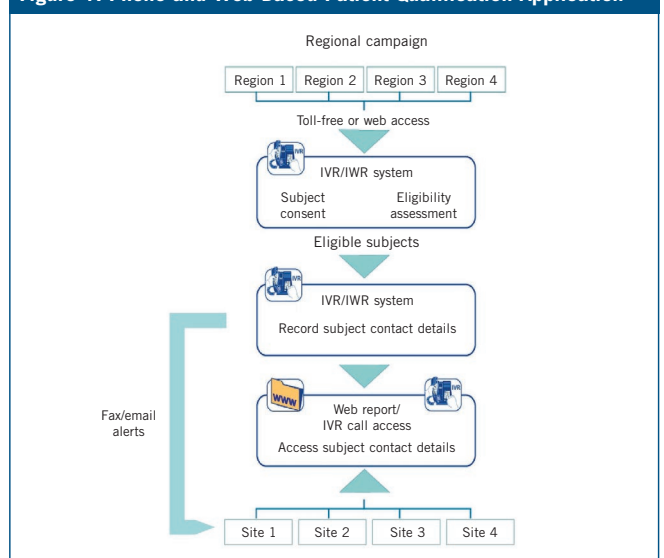
Investigators, sponsors and CROs can undoubtedly improve recruitment and retention. Several areas for improvement are demonstrated by the following metrics. Only 21 per cent of potential volunteers who respond to generalised searches (such as untargeted advertising) fulfil basic inclusion and exclusion criteria. Moreover, on average only 73 per cent of recruited patients remain in a trial until completion (1). Indeed, some 70 per cent of sites fall short of their recruitment target, many failing to recruit a single subject (2). Against this background, CROs and clinical technology companies have implemented a variety of strategies to optimise recruitment and retention. This article examines two of these approaches: interactive voice response (IVR) and interactive web response (IWR).

OBJECTIVES OF A PATIENT RECRUITMENT CAMPAIGN

Patient recruitment campaigns have several objectives. In all studies, the campaign aims to recruit subjects within a defined time – ideally as short as possible – while managing the throughput of potential volunteers to study sites. The campaign should also ensure that subjects screened by the investigators are highly qualified, which reduces the number of volunteers that fail screening on site. This makes efficient use of the investigators' limited time.

When using IVR and IWR, patients respond to advertising campaigns by telephoning a toll-free number or accessing a secure website – the URL and phone number being displayed as part of the advertisement. Candidates responding by telephone (IVR) hear

Figure 1: Phone and Web-Based Patient Qualification Application



several pre-recorded voice prompts that are specific for each protocol. The candidate responds to questions using the telephone's touch-tone keypad. IWR uses a secure Internet site to allow potential patients to complete the study-screening questionnaire. Since patients are initially guided to the online screeners via traditional advertising (such as radio, newspaper, posters and so on), this method is not pure web-recruitment; however, IWR can be used as an interface to qualify candidates who are attracted when a campaign uses the Internet as a media platform. Typically, IWR offers an alternative to the telephone for candidates reached by a variety of conventional media types. Giving candidates a choice of response channels – such as phone or web – tends to achieve higher response rates. Figure 1 (page 56) details the way in which the IVR/IWR application is used to filter and direct candidates in a typical media-based recruitment campaign.

Before completing the candidate screener, it is vital to gain the potential patient's consent so that the information may be used for the recruitment campaign. Their consent is obtained by pressing a button on their touch-tone keypad or ticking a checkbox on the secure website. Following this, the study-specific screening questionnaire is delivered. The aim of this is to qualify or disqualify candidates as accurately as possible, and this may include complex computerised clinical assessments. Candidates qualifying are asked to leave their contact details; those disqualified are usually given appropriate information about where to find help for their condition. Based on the patient's location, the system automatically alerts the nearest clinical site and saves the contact details in the site's queue. When a site has qualified candidates in the queue, the system issues a fax or email indicating that there are new contact details to access. For records collected using the web, the contact details can be sent immediately to the site via fax or email. For those collected using the phone, site-staff make a toll-free call to listen to the contact details. It is usual for sites to make the contact with qualified candidates to arrange formal screening appointments, but this can also be facilitated by a third party operator. In addition to providing campaign metrics, the system can also report the speed at which subject contact details are accessed by study sites, providing the clinical research associates (CRAs) with a measure of site workload or motivation issues.

Because of the untargeted approach of many media platforms, qualifying candidates before passing them on to a study site is vitally important. IVR and IWR technology offers the ability to incorporate complex diagnostic screeners, clinical assessments and scoring algorithms to determine candidate qualification, as illustrated in the case histories featured later in this article. Furthermore, during the study, IVR can collect data for patient diaries, quality of life and health economic assessment. Volunteers find IVR a straightforward way to input information: in a survey of 449 patients using IVR, 92 per cent found the system 'easy-to-use' and 77 per cent indicated that it was 'very easy'.

The campaign doesn't end when the requisite number of volunteers is enrolled. Ideally, the campaign should aid patient retention by supporting sites and patients during the study. Furthermore, the

campaign should also encompass site management tools and reports that allow the sponsor to review recruitment in real-time. Solutions like IVR and IWR allow such real-time analysis of recruitment by total number as well as stratified by site and patient

Case Studies

A growing number of studies now realise the potential offered by IVR and IWR in patient recruitment and retention. Indeed, the technology has been used for therapy areas as diverse as psychiatry and gastroenterology. The following case histories exemplify this potential.

Multinational Application

In combination with the sponsor and patient recruitment firm, an IVR screening application was developed to qualify candidates responding to local radio and newspaper advertising, clinic posters and leaflets across Europe, Australia and Canada. For this sensitive disease indication, the IVR screener asked very personal questions and included a complex clinical assessment instrument that assessed disease severity. The IVR application was delivered in local languages.

All the ethics committees involved accepted IVR as a means to pre-qualify candidates. The IVR recruitment system received over 3,000 calls and provided over 300 qualified candidates to site (11 per cent). The study recruited within 12 months of the start of the advertising campaign; 90 per cent of candidates were obtained from advertising. IVR was particularly effective because of the sensitive nature of the screening questions. IVR also delivered standardised clinical assessments of disease severity, which limited the number of screening failures on site.

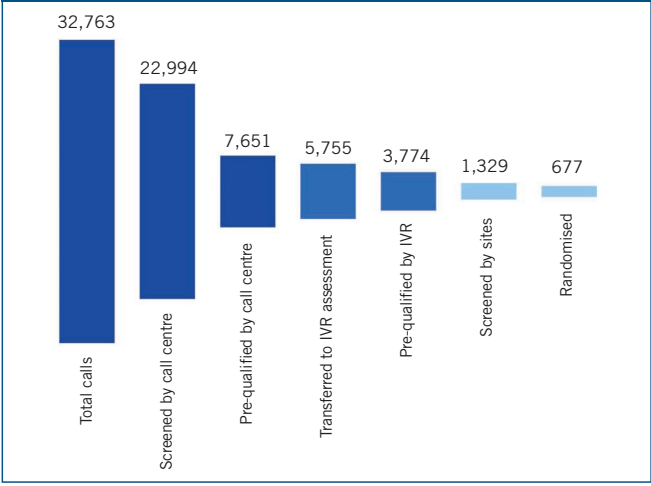
Complex Clinical Assessment

Although IVR and IWR offer an alternative to call centres, the two approaches can be integrated. For example, two studies on depression enrolled 700 patients from 150 sites in the US, using conventional clinic referrals and direct advertising in the press and on the radio. Qualified call centre personnel answered patients who responded to the direct advertising by calling a toll-free number. Operators gave brief study information, took the candidate's consent to answer the pre-screening questions, assessed respondents against basic entry criteria and recorded contact details.

Consenting candidates were transferred to the IVR system, which used a validated computerised interview to assess prospective patients against the 17 items of the Hamilton Depression Rating Scale (HAM-D). The study aimed to enrol patients with a total HAM-D score of 20 or greater. Candidates were then transferred back to the call centre where the personnel put qualified subjects in touch with sites for formal screening.

Direct-to-consumer advertising recruited 43 per cent of patients. Of the 32,763 individuals who called the toll-free number, 7,651 passed pre-qualification by call centre interviewers. Of these, 3,774 met the diagnosis and severity eligibility criteria specified by the IVR structured interview. Of these, 1,329 consented to be screened and 677 were enrolled (see Figure 2). This example shows that pre-qualification using a standardised clinical assessment can improve the quality of site referrals and increase patient throughput. In one of the two depression studies, the sponsor estimated that this approach halved the recruitment period (3).

Figure 2: Candidate Response Funnel



subgroup, such as ethnic minorities, the elderly and women. This allows the sponsor and CRO to proactively address any problems in recruitment, such as sites that are not attaining the targets.

Real-time reporting also means that the sponsor can determine which recruitment strategies are the most effective and tailor the media buying to the most appropriate or cost-effective media. For example, system reports can summarise common reasons for candidate disqualification, enabling the sponsor to re-examine study inclusion and exclusion criteria. The reports may also show insightful figures such as response rates of various demographic groups broken down by media platform. For example, if a study is recruiting too few subjects in important cohorts, buyers can target media that reach these groups more effectively.

Furthermore, sophisticated IVR and IWR applications may be configured as simply two interfaces with a common database, enabling integrated reporting between the two channels. In studies using IVR/IWR applications to perform study randomisation, it is possible to link qualified candidates from the recruitment campaign to randomised or screen-failed subjects, and for those randomised, to identify whether they completed or withdrew from the study early. This provides powerful metrics measuring the performance of a recruitment (and retention) campaign.

Whether potential patients use IVR or IWR, the direct input means that the system automatically records the patient's consent and details. Phoning a call centre, on the other hand, introduces another element in the process – the operator – that can result in transcription and other human errors. In fact, it can be difficult to obtain campaign metrics and reports quickly and accurately when using a call centre. Using multiple call centres in a single study exacerbates this problem. Integrated real-time reporting automated by the IVR/IWR approach allows the sponsor to have all the necessary metrics at their fingertips – and accuracy is assured.

CALL CENTRE LIMITATIONS

IVR and IWR allow sponsors and sites to optimise recruitment in a number of other ways. For example, IVR and IWR effectively channel responses to advertising campaigns, while overcoming some of the limitations inherent in call centres, such as:

- ◆ Call centre operators often need intensive training and an ongoing audit in order to ensure accurate recording of data and standardised qualification of patients. IVR and IWR overcome these problems. A technological approach guarantees that all patients are assessed in a standardised way.
- ◆ Some potential patients may be reluctant to phone a stranger to discuss a medical condition. This problem is especially pressing when the condition is sensitive, emotional or embarrassing, such as sexual health. Such reluctance may be especially widespread in certain cultures. IVR and IWR, on the other hand, are anonymous.
- ◆ Using a call centre for a multinational study can create problems if potential volunteers could speak one of

several languages. The cost of recruiting additional language specialists within a call centre, or running several centres in the various countries, is often considerable. In contrast, IVR and IWR can be tailored to cost-effectively run questionnaires in unlimited languages.

- ◆ A high call volume – which is typical in some therapeutic areas, such as AIDS and HIV – can overwhelm the call centre. Being put on hold can put some people off. There is, in essence, no limit on call volume using IVR and IWR systems.

Data protection is obviously a concern for regulatory authorities and sponsors. IVR and IWR, however, offer unprecedented data security – indeed, by their nature, IVR and IWR are more confidential than using an operator at a call centre. A secure central database stores the information received from IVR and IWR. Access to the system is restricted to trained personnel and, although with candidate consent can be retained longer, the database typically retains personal information only for as long as is needed to contact potential patients regarding the current clinical trial (for example 28 days).

Furthermore, potential volunteers consent at several stages, which offers further data protection. Apart from consenting to answer the medical questions contained in the qualification questionnaire, qualified candidates agree that their contact details can be passed on to the study site. Data protection requires that subjects consent to the potential uses of their data, and (as with a call centre managed campaign) this ultimately requires that the sponsor is contractually responsible for ensuring that sites only use patient contact details for the purpose of potential recruitment into that study.

CONCLUSION

IVR and IWR provide an efficient, multilingual channel to screen patients who respond to media advertising and other forms of recruitment. IVR and IWR facilitate the delivery of standardised, complex clinical assessment instruments. This pre-qualification improves the quality of site referrals and increases the throughput of patients. Overall, IVR and IWR can help sponsors and CROs optimise patient recruitment and retention, which should help companies maximise the return on investment. ◆

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