Pick and Choose

Traditional methods of finding suitable candidates for clinical trials are time-intensive and cost drug companies millions, putting the development of new medicines at risk and elevating prices. New techniques borrowed from big data analytics allow the process to be completed much more efficiently

Tigran Arzumanov, Bernhard Bodenmann and Le Vin Chin at Clinerion

The search for patients with suitable profiles to participate in clinical research drug trials has been compared to the proverbial search for the needle in the haystack – and rightly so. Traditionally, the call would go out from the pharmaceutical drug developer to their local affiliates, who would contact their friendly local hospitals, where diligent medical researchers would comb their paper-based patient records for candidates who fit the long list of inclusion and exclusion criteria – a laborious, time-consuming and costly process.

The identification of trial-eligible patients represents a considerable and costly bottleneck for the industry, impacting patients directly in the form of slow progress and availability of new drugs on the market, as well as elevated prices as a result of longer development time and shorter patent protection. Each day a drug is delayed from reaching the market, the pharma company loses up to $8 million (1). Recruitment difficulties are the underlying reason for 30% of Phase 3 terminations (2). Almost half the sites (48%) miss their enrolment targets for Phase 2 or 3 studies, with timelines nearly double their originally planned duration to meet desired enrolment numbers (3). The level of inefficiency and waste is, therefore, considerable.

Electronic Health Records

The advent of electronic data capture and electronic health records (EHRs) has only slightly improved the situation. A hospital's health information system (HIS) is not optimised for patient search and identification within the context of a clinical trial, and there are often no structured tools available. Even if there were, these systems generally have limited search functionality; a user would search for 1-3 parameters, and then resort to a manual verification of the remaining criteria.

Outside patient recruitment, information technology has been applied in clinical research for over 50 years. Nowadays, electronic data capture has become the de facto standard in trials. Statistical randomisation technologies are used in planning studies centrally, and allow the trial manager to minimise bias by creating comparable cohorts across study sites. Meanwhile, drug shipments are managed by software that calculates the optimal location of warehouses, time spent in transit, supply expiry dates and site stock.

Clinical trial management systems have been developed for the use of both pharma companies who sponsor clinical trials, and CROs that often manage their execution. These systems control data collection and the actions of clinical research associates (CRAs) and doctors, calculate site invoices to sponsors based on patient procedures, and allow the aggregation and review of data on CRA and patient visits.

There have been some attempts to use electronic systems for patient recruitment, but more in the area of engagement – finding and approaching patients directly through channels such as online groups and social media, and inviting them to join trials. This approach works well for studies that rely on volunteers, who are motivated to participate in clinical trials and are more suited for chronic clinical conditions. However, direct-to-patient marketing is labour-intensive and can result in high numbers of irrelevant leads.

Patient recruitment based on EHRs is, to date, a neglected and under-utilised area. Individual HISs have attempted to conduct patient recruitment based on their EHRs, but multi-hospital networks did not exist until very recently.

Brief History

Electronic records for patient data came into use with the advent of digital technologies. Hospitals and doctors' practices recognised the value of keeping patient records electronically for the documentation of patient encounters in a standard and consistent way, reducing the problem of illegible, hand-written notes and improving care by ensuring transition of care and continuity of treatment. These records became known as electronic medical records (EMRs). EMRs took root very easily because they enabled data to be stored efficiently and retrieved quickly within a practice, while maintaining specifiable standards of data security, safety and retention.

At a higher level, clinical information systems – which went across practices and allowed the integration of patient information from multiple sources – arose in the 1960s. These became more standardised in the 2000s, and became known as EHRs. A patient's complete medical history – including results from external labs and diagnoses from specialists, for instance – EHRs compile an overall picture of a subject's health, while also supporting the management of patient

information within the healthcare ecosystem. As a result, EMRs/EHRs enable doctors to offer a better standard of care for their patients.

Feasibility

Representing a rich source of patient information, a moderately structured EHR allows complex queries to be made to a patient database – taking account of, for example, medical history, medications taken, procedures and lab values. A sponsor may, therefore, use such a query to evaluate the possible number of patients at a specific hospital which fit a specific set of criteria – and thus evaluate the feasibility of that site to run a specific study. A mistaken feasibility assessment would represent a potential source of problems, such as a trial not taking off, if the patient enrolment numbers cannot be met; or an unnecessary number of small studies in numerous locations, due to inefficient siting of trials.

EHR use allows the standardisation of the feasibility evaluation across multiple sites and, to a considerable extent, removes the subjective element from the process. However, the employment of EHR data across hospitals, healthcare networks and countries has a number of associated challenges, including inconsistent coding practices and semantic interoperability. These issues can be identified and mitigated, though – something that is much harder to do with subjective recruitment estimates by individual principal investigators, known to provide patient enrolment estimates that may not meet the expectations.

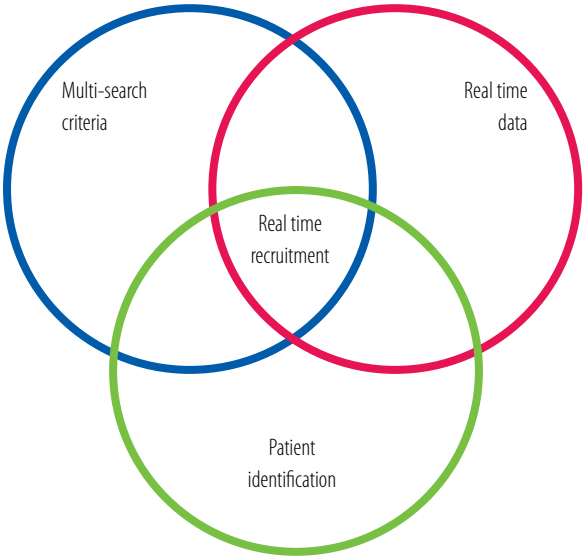
Identifying Patients

Performing feasibility studies through EHR-networked hospitals allows sponsors to identify the most suitable research hospitals for their trials, but gives doctors no tool to find the patients. By itself, feasibility can be a poor predictor of a study's success, as the sites will still be limited in their ability to identify the relevant patients in time – for example, if the trial requires a patient profile where dozens of criteria overlap, or where studies are for acute indications which cannot be predicted from historical information, or especially if the trial is time-sensitive.

An EHR-based recruitment system that can identify patients allows a trial's primary investigator (PI) to start a study with a ready-to-use list of patients to screen, potentially generated already from the feasibility query. This reduces the PI's workload dramatically and accelerates trial progress. It also facilitates recruitment targets to be met more easily – particularly in difficult cases, such as studies where patient consent is very low, or rare diseases.

This is where the benefits of EHR-based patient recruitment become apparent. Querying a complete database electronically enables all potential candidates who fit the trial protocol criteria to be found – exhaustively, and within a short time. The fact that the candidates are pre-filtered according to matches with the protocol also helps the subsequent processes of candidate validation and enrolment. This reduces the time and resource effort from the beginning, allowing the trial's PI more flexibility in managing the trial and completing it on time, or even earlier than expected.

Figure 1: Successful patient recruitment requires the identification of sites according to how their patient populations fit multi-search criteria, the identification of patients which meet the study criteria, and the ability to do both in real time



The ability to run a query against multiple overlapping recruitment criteria not only enables a trial manager to come up with a better defined patient population distributed across multiple sites, but also brings the capability to run studies in populations which would normally be associated with personalised medicine. Sometimes, these criteria are so specific that eligible patients may only be found on a level similar to rare disease populations – for example, in fewer than 100 patients per million.

Patient Enrolment

Depending on how they are configured, electronic recruitment systems may screen for patients on a continuous basis and identify eligible candidates in near-real time. This offers another important advantage where trials are time-sensitive. Recruiting a patient may depend heavily on certain criteria which have a shelf life: for example, if a specific lab test has to have been done within the past 24 hours, or if a specific treatment has to have been initiated in the last seven days. Real time systems allow such criteria to be queried, and a candidate population to be assessed against completely up-to-date patient information.

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But the beauty of real time systems lies in their potential to support the search for patients with acute indications, where historical data are of no help. In these indications, the search is for patients where there are no predictors for their condition, and relies on the patient arriving at the site on occurrence. A good example would be trauma studies. The time between the appearance of the patient and the start of standard treatment would usually be very short, and it is a major challenge for the PI to include the patient in a clinical trial without a system that identifies the patient upon arrival and alerts the clinical researcher immediately.

Real Time Recruitment

Bringing everything together, a subset of studies can be identified which require three distinct candidate search capabilities to arrive at successful patient recruitment. They include the identification of sites according to how their patient populations fit multi-search criteria, the identification of patients which meet the study criteria, and the ability to do both in the very limited amount of time available from the moment the data appears in the system – ideally instantly (see Figure 1, page 49). The confluence of these three features is where the strengths and benefits of real time recruitment become possible.

Examples of indications that could benefit from real time recruitment include trauma surgery, acute infectious diseases, pain relief and certain acute cardiovascular conditions, which require time-sensitive treatment initiation.

The implementation of a real time recruitment system is not without challenges, however, as it heavily depends on the ability and readiness of investigators to use it. Responding to an alert requires quick, coordinated action within the research team. Acute indications are normally treated with urgency, but using traditional techniques means PIs may not be aware a suitable patient has come in until the window of opportunity is gone. Therefore, PIs and study staff need to have quick and ready access to the relevant information, and be able to set up procedures for referral, enrolment and consent for patients for acute indications studies.

Enrolling Patients Successfully

Multi-site feasibility and patient identification in real time, with alert generation, is an indispensable tool in modern clinical research, allowing the successful enrolment of acute patients corresponding to complex recruitment profiles.

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About the authors

Tigran Arzumanov, PhD, MBA, has been working in the area of Clinical Research Sales and Marketing since 2004, and has extensive experience in commercial aspects of both pharma research services and eClinical solutions.

Email: tigran.arzumanov@clinerion.com

Bernhard Bodenmann, PhD, is experienced in Requirements Engineering and System Architecture of eClinical solutions and has been working in clinical R&D since 2006.

Email: bernhard.bodenmann@clinerion.com

Le Vin Chin has been working in Marketing for 20 years across a wide variety of industries, including software and services.

Email: levin.chin@clinerion.com