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BRIEFING NOTE

Clinerion's Patient Recruitment System (PRS):

A big data solution for patient recruitment for more effective and cost efficient clinical trials

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Executive summary: Overcoming the challenges of clinical trial recruitment using big data technologies

The problem defined

Any prospective new drug must successfully pass a succession of three clinical trials phases, before it can apply for market approval. These trials represent a significant investment for a pharma company and, as they are prone to delays and can even fail altogether, they put immense financial pressure on them.

One of the root causes for the failure of trials is the inability to recruit the specified number of eligible patients in the foreseen time span. Delays in the market launch can amount to as much as US$8 million per day for a blockbuster drug in opportunity costs for a pharmaceutical company.

Today, eligible patients are still mostly identified by manually scanning physicians' patient lists. But this is not only a time consuming, resource-intensive and lengthy procedure, it is also far from fool proof. Many suitable candidates may be missed.

A viable and effective solution: automated patient recruitment

The proposed solution takes advantage of an emerging trend to digitise patient records at hospitals, which means that hospitals have a database of patient information in more or less real-time. An electronic solution which can (indirectly) query this data can obviate the above procedural problems. This results in a more efficient and effective recruitment process, that takes less time, frees up resources and is rigorous in matching patients to protocols. All this, ultimately, leads to a faster launch of new therapies.

Clinerion: A compelling patient recruitment system provider

Swiss software solutions vendor Clinerion's mission is to improve the efficiency and quality of the traditional patient recruitment process. Its Patient Recruitment System (PRS) facilitates the electronic selection of trial sites and the recruitment of patients, by screening hospital patient data in real-time. PRS optimises and accelerates the clinical trial process in modules, which helps to optimise the study protocol, select high-potential trials sites and find more eligible patients in a shorter time period. On average, PRS finds 10 to 30 times more patients, faster, compared to manual screening.

PRS works by screening the electronic health records (EHRs) of networked partner hospitals that are located in diverse geographies. In doing so, it reaches millions of candidate patients in those institutions. Although each hospital's database may have a different structure and may be supplied by a different systems vendor, the patient records from the multiple sources are made interoperable by a set of mapping and semantic methodologies.

A process of patient ID pseudonymisation, the placement of queried servers within a hospital's own premises and the use of a distributed cloud network ensure patient privacy.

PROOF POINT

Hospitals using PRS report more efficiency in running clinical trials, with a significant reduction in time and resources needed to conduct clinical studies:

"Before using PRS, we needed two hours to screen 100 patients and only three or four of them would be qualified. However, finding three eligible patients with PRS took only five minutes."
Istanbul University Hospital.

With more patients recruited in trials, hospitals also generate higher revenues from trials:

"We get more patients, which means more income"
Istanbul University Hospital

As a result of the efficiency increase, occasioned by PRS, and of the higher exposure to Clinerion's international clients, hospitals in the PRS network have a higher likelihood of participating in leading-edge sponsored trials, which can improve their academic reputation and increase institutional revenues.

Making the case for PRS: Balancing clinical trials with business needs

Before a new drug can be launched on the market, it needs to go through a set of three consecutive clinical trial phases that assess the safety and efficacy of a newly developed medicine on humans. However, less than 40% of these trials are completed successfully.[1]

A major factor in the success of a trial is the patient recruitment process. This is because the identification of the specified number of eligible patients who meet the ever more complex inclusion and exclusion criteria, within a given timeframe, can be a considerable hurdle. In Phase 3 trials, where the size of the study sample is significantly larger than in the two previous stages, having sufficiently large patient numbers is especially vital.

[1] Chahboune, Pharm, Ind. 77, Nr. 2, 173-180(2015)

Assessing the real costs of poor patient recruitment

An analysis of more than 100 trials established that just under one-third of them did not meet their recruitment target and half needed to prolong the recruitment period to fulfil this target. [2] Delays in recruiting the required number of patients at an investigator site can compromise a trial's statistical power and scientific validity. It also means that the availability of potentially beneficial treatments to the public is postponed.

Difficulties in patient recruitment often results in delays and, in the worst case scenarios, the actual cancellation of a trial.

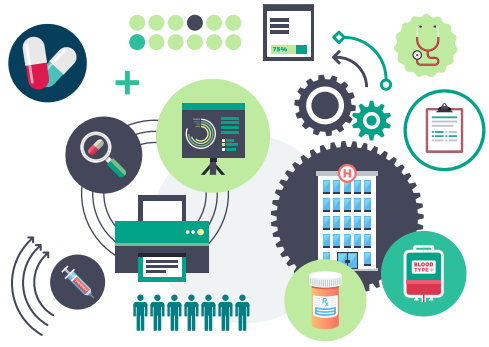
Every day that a drug's launch is delayed comes at a high cost for a pharma company. Missed sales for a blockbuster drug can amount to an estimated $8 million (USD) and up to $600,000 (USD) for a less popular product.[3] All of this can add to the overall development cost for a pharma company.

Clearly, it is in the interest of the pharma companies to render the clinical trial process more efficient and less costly. And since patient recruitment represents, on average, about 30% of the overall time required for conducting clinical trials, making this area work faster and more effectively will help achieve this. There are, of course, other additional costs factors that need to be tackled, such as regulatory and administrative barriers and the growing competition for qualified investigators and sites. However, these are not in the remit of this paper.

Resolving the pitfalls of recruiting patients into clinical trials

Patient recruitment is not a single activity, but an array of tasks that include, among others:

- **protocol development**: setting the profile of eligible candidate patients
- **site feasibility checks**: determining the potential number and location of eligible candidates
- **site selection**: setting the trial site strategy
- **patient enrolment**: screening of patients and obtaining their consent to participate in the trial.



To enrol patients, there are various methods of patient screening. However, the predominant one is to cooperate with healthcare providers, especially hospitals. This allows investigators to tap into the existing pool of patient data archives. Nevertheless, if done manually (still the prevailing mode) it is highly labour intensive and time consuming and, therefore, expensive. Moreover, its results are not always reliable – mainly due to a lack of medical knowledge and / or insufficient understanding of the research protocol, from those who conduct the scanning.

It is true that the growing digitisation and consumerisation of healthcare have helped to overcome some of the speed and efficiency limitations of traditional, manual patient recruitment methods and provided the scale to reach the wider population. Examples include the use of social media, patient networks (e.g. PatientsLikeMe) and advocacy groups (e.g. the Multiple Sclerosis Society), which allow patients to self-identify themselves within communities that are potential recruitment grounds for trials. Meanwhile, the patient engagement and retention work of third-party patient recruitment service providers (e. g. Acurian, Synexus) is another means to render the trials process more efficient.

[2] McDonald AM, Knight RC, Campbell MK, Entwistle VA, Grant AM, Cook JA, Elbourne DR, Francis D, Garcia J, Roberts I, Snowdon C: What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. Trials. 2006, 7: 9-10.1186/1745-6215-7-9.
[3] ISR-The-Expanding-Web-of-Clinical-Trial-Patient-Recruitment%202014.pdf

But it is the growing availability of electronic patient data that, potentially, has the biggest positive impact on patient recruitment. It paves the way for a more efficient and scalable recruitment process, as well as speeding up the screening of eligible candidates.

The adoption of hospital information systems (HIS) to capture data, generated during patient care, including those from EHRs, has made the identification of potential trial subjects significantly more efficient, as it allows the pre-selection of patients for specific trials, based on their disease status and individual characteristics. An automated notification system can alert study teams at a hospital when suitable patients become identified, so that the team can then retrieve the up-to-date list of potentially eligible candidates from the HIS. In a next step, authorised access to the patient's full EHR can allow the study team to retrieve additional information, in order to verify their eligibility. Once done, a study physician can then seek consent from the patient to participate in the trial.

Having the means to screen, not just one, but multiple healthcare institutions– even across different countries – for eligible patients would further shorten the overall time needed for patient recruitment. To this end, a platform is needed that uses real-time data from EHRs and can access multiple HIS types. Provided it complies with privacy and other relevant governance and security policies, patient screening can be done in a fraction of the time needed for the manual screening process – and with improved results.

Clinerion's PRS explained

Clinerion's PRS solution facilitates the automated recruitment of patients and allows for an optimal selection of trial sites, by using up-to-date EHR data. The solution can be deployed in all types of hospitals and for all disease indications in interventional and observational trials.

Clinerion's PRS helps accelerate the clinical trial process by:

- **Optimising protocols:** By optimising the number of potential patients for a protocol query in PRS's Protocol Designer tool, the feasibility of a study can be evaluated. In this way, study teams can easily validate or adjust the selection criteria of a study protocol, prior to its approval.

- **Selecting high-potential trials sites:** By running a query in PRS's Site Finder tool across the up-to-date patient records of all hospitals in the PRS network, a trial sponsor can determine the distribution of potentially eligible patients – and can then decide which sites to approach.

- **Finding more eligible patients faster:** Based on results to date, PRS finds 10 to 30 times more patients, compared to manual screening and in a significantly shorter time span. Due to this, PRS can facilitate the recruitment of patients for time-critical trials. For example, patients suffering pneumonia, who would otherwise be treated immediately with conventional therapies, can be directly enrolled into a clinical trial, as PRS's Patient Finder tool notifies primary investigators and study nurses at trial sites about potential candidates in real-time.

- **Enabling more innovative studies to be conducted:** Due to more efficient processes – i. e. being able to focus on patient enrolment, rather than on patient identification – and a higher number of patients recruited, trial sites can run more studies and increase their reputation for high performance.

Outlined below are four important features underpinning Clinerion's PRS solution:

1 **Clinerion installs** a server within a hospital's IT infrastructure, on which patient data from the HIS is loaded. Having first been anonymized and pseudonymised, the data is then put through various key processes, such as semantic enrichment, terminology-mapping and clustering processes, before being indexed. It is this indexed information that is then queried by PRS.

2 **PRS is a hybrid** cloud- and federated-installation-based platform. The cloud delivers the queries to the federated installed servers at the hospitals and the results (the count of patients who match the criteria) are returned for aggregation in the cloud. In this way, no patient data leaves the secure environment. The cloud contains no patient data, just 'data about data', meaning that the PRS Cloud cannot be hacked for confidential information. This federated system also makes it very easy to include new partner hospitals. The querying of the indexed data can happen within seconds.

3 **PRS allows a study** protocol's eligibility criteria to be put into a structured, computable form that then can be delivered via cloud to query local installations.

4 **The eligibility** criteria are mapped between all standard medical and hospital-specific terminologies, using semantic / ontology-mapping methods. In this way, patient conformity to eligibility criteria can be evaluated, regardless of differences in terminologies, which is particularly important in the case of global trials.

These four features constitute a system that can query and aggregate patient information, across multiple local installations, within a network of hospitals, across different geographies, and without compromising patient privacy. As more and more hospitals install PRS, the PRS-hospital-network will grow – and with it the pool of suitable candidates.

Once installed, PRS is controlled by a site's own IT department. To ensure privacy and security of patient data, the latter is pseudonymised and patient IDs can only be re-identified by authorised personnel on a hospital's premises, via PRS's Patient Finder tool. Each site controls the pseudonymisation, to ensure that no unauthorised re-identification of patient IDs can be performed. As soon as a patient who matches eligibility criteria is identified, the respective study team will be notified by SMS text, Instant Messaging or email.

Proven benefits for hospitals using PRS

Launched in 2013, PRS has acquired a growing network of partner hospitals that permit real-time access to their anonymised patient data. The partner hospital network comprises research-heavy hospitals in Turkey, with a total current patient catchment area of around 30 million.

Those hospitals using PRS have benefited from more efficiently run clinical trials, resulting in a significant reduction in time and resources needed to conduct clinical studies. Furthermore, with the assistance of PRS, the hospitals are now in a position to improve their trial revenues, as well as their academic reputation.

Summarised key benefits have been:

- **More efficient use of staff:**
  - PRS facilitates a smooth validation and adjustment of the study protocol criteria. It shows how changes in inclusion or exclusion criteria in a study protocol can affect recruitment.
  - No further need for investigators to estimate the numbers of eligible patients to establish the feasibility of a trial.
  - Study teams can generate lists of patient candidates in a fraction of the time, compared to manual research.
  - Only limited ongoing IT support from the hospital's IT staff is needed, as Clinerion maintains the PRS system.
  - Queries can be run by the clinical staff, with no additional IT support needed for coding.

- **Exposure to more trial opportunities expanding a hospital's revenue base:**
  - The successful running of clinical trials positively affects the bottom line, as each participating patient increases study revenues. With more patients available for each trial, overall trial revenue grows.
  - PRS checks patient availability before putting a hospital forward for a trial, which increases the probability of a hospital meeting and exceeding the recruitment target.
  - As PRS identifies patients in real-time for inclusion in trials, as soon as they enter the hospital, it facilitates the running of time-critical trials.
- **Increased academic reputation:**
  - Being part of a network of hospitals using PRS increases the chance to partake in cutting-edge sponsored trials.
  - PRS supports a hospital's academic and internal trials at no additional cost. This increases its chances of publishing more scientific papers and being invited to international scientific conferences. It also helps a hospital to attract high-calibre researchers.

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