How EHR-based Recruitment and Retention supports Patients Centricity

PEER REVIEWED

A renewed focus on the needs and the experiences of patients is welcome, and has been shown to make drug development and launch more effective. But how is "patient centricity" to be effected? We analyze particularly how patient data, in the form of hospital electronic health records, offer a data-driven entry point into patient centricity, making trial participation more easy, democratizing patient engagement, and accelerating trial recruitment and enhancing retention.

The Rise of Patient Centricity

Patient centricity has arisen from the idea that the development of new treatments can be better done by redesigning its processes around the needs of patients, and calibrating treatments to the wealth of knowledge of their experiences as patients living with illness. Patient centricity also has its roots in recovering the idea that the betterment of the patient's health is the fundamental point of drug development, and decrying the pharma industry's approach based on 20th century industrial business processes.

"Too often, trials and studies are conducted to support new products or patents rather than patients," says Parkinson's patient advocate Benjamin Stecher. He calls for reform, pointing out that the "average patient" is a statistical construct rather than a physical entity and asking us to consider that, for Parkinson's, therapeutic development cannot move fast enough to keep up with a patient's neurodegeneration, nor deal with variability between individuals[1]

Placing the patient as the center of clinical and medical development is therefore advantageous, as it simplifies the patient journey and thereby improves patient involvement and engagement during drug development. The pharmaceutical industry is a juggernaut that moves at its own majestic pace; the refocusing on the patient as the alpha and omega allows the drug development process to be steered more nimbly.

And, indeed, patient centricity is on the rise around the world. Analysis in 2019 conducted by Informa Pharma Intelligence, using data analytics provided by Trialtrove® and Pharmaprojects®, shows that patient-centric trials have been on the increase, reaching an apparent peak of patient-centric trials completing in 2016. The analysis also shows that patient-centric trials are well-distributed around the world (Figure 1)[2].

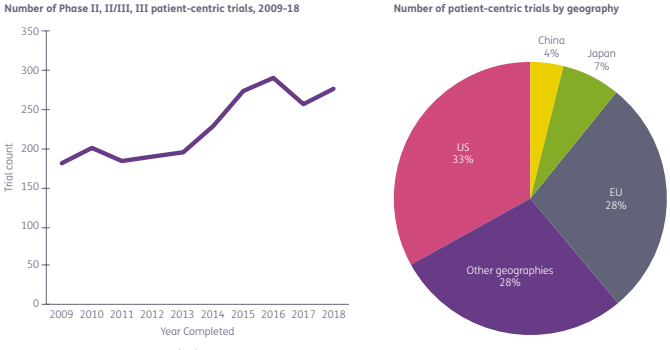

Figure 1: Analysis on Trialtrove® data shows that patient-centric trials have been on the increase, and are being run around the world.

Patient Centric Trials

Patient centricity doesn't just benefit the individual patient. The same analysis shows that drug trials designed to be patient-centric were more successful – they had a higher likelihood to launch (74%, compared 54% without patient centricity – a whopping 20 percentage point difference) (Figure 2).

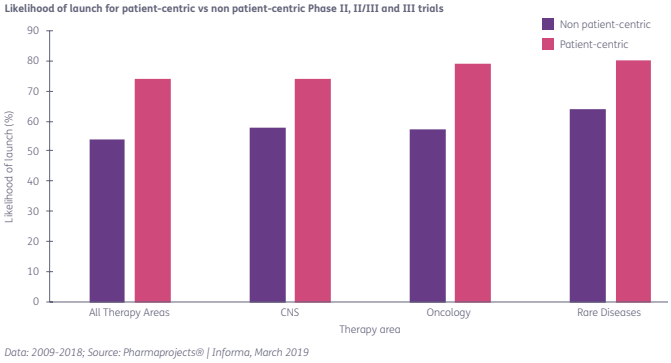

Figure 2: Analysis on Pharmaprojects® data shows that patient-centric trials have a higher likelihood to successfully proceed to drug launch, across multiple therapeutic areas.

The success of a trial relies very much on having enough patients in a trial for the results to be statistically meaningful. By giving patients a better understanding of medical and clinical issues, and making it easier for patients to participate, patient-centric trials offer a notable advantage in achieving trial recruitment targets quicker (in the analyzed population, there was an average 3 months' reduction, from 6.5 months to 3.2 months, to reach enrolment of 100 patients) (Figure 3).[2]

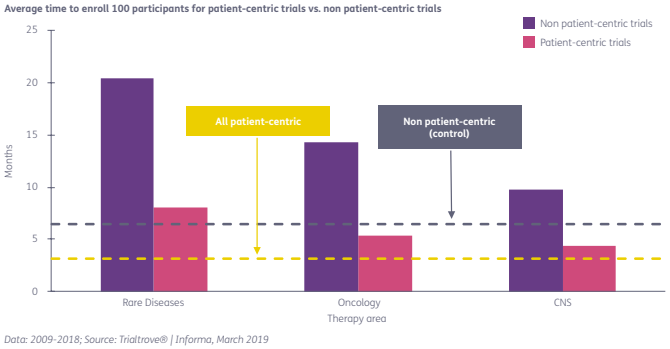

Figure 3: Analysis on Trialtrove® data shows that patient-centric trials get 100 participants enrolled faster, most notably for rare diseases.

Throughout recruitment and beyond, engagement and retention are the drivers for successful trials and the next steps that can be addressed with a patient-centric approach. A recent survey by SCORR and Applied Clinical Trials shows that 68% of respondents (55% from the USA and 29% from Europe) believed that patient engagement would increase in their own companies within the next two years and the main engagement goals were "adherence to dosing and visit schedule," "higher retention rates" and "satisfied patients." [3]

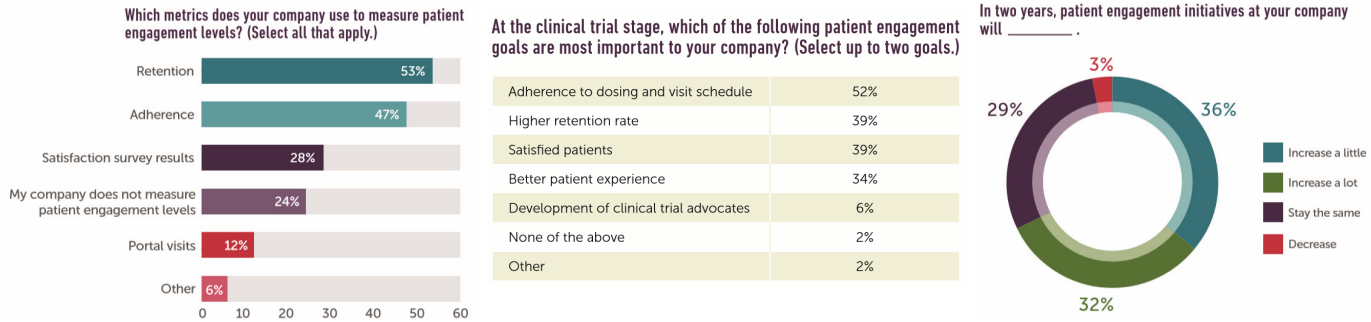

Figure 4: a survey by SCORR + Applied Clinical Trials shows that engagement and retention are crucial during the clinical trial stage.

That engagement and retention can be supported by understanding a patient's experience and needs better would seem self-explanatory. A pharma company's need for "understanding the patient journey in clinical programs begins with looking at the therapeutic area you are studying and understanding what patients who suffer from the disease being studied go through. Then asking how you can make participating in your clinical study a little bit easier for them."[4]

The Patient Experience and EHRs

When it comes to understanding the patient experience, the main tools are surveys, interviews (and focus groups) and patient shadowing. In this article, we would like to focus on how querying of de-identified patient electronic health records (EHRs) can provide its own trove of data on the patient experience, particularly the patient journey and outcomes. EHRs are de facto patient-centric, and analysis of EHRs can offer key directions for recruitment, engagement and retention.

As for whether they also contain the data which is needed to illuminate the full patient experience, the answer depends on what data should be gathered for evaluation. According to LaVela *et al*, "a key component of a successful strategy for understanding and improving patients' experience is ensuring that what is measured reflects what matters most to patients" and "consideration must be given to whether the metrics and measures that are being used are sufficiently capturing patients' experiences."[5]

EHR analytics are perhaps the only truly live way for pharma to access patient experience. Every other technique is a snapshot in time, limited by parameters specific to the investigation being conducted. Analyzing EHR, queries can be created on the fly, hypotheses may be formulated and tested in real-time, alternate patient pathways can be assessed and evaluated based on real patients. In this way, it is possibly the most important starting point for the pharmaceutical industry to understand patients.

An advantage of EHRs is in the ever-evolving and improving complexity of artificial intelligence (AI) and most importantly Natural Language Processing (NLP) in understanding text strings written by human beings. As technology progresses, we expect that doctors' notes will become more comprehensible by AI running natural language processing algorithms, making free-text notes in EHRs searchable. This will unlock a wealth of patient experience data.

EHR Pillars to Patient Centricity

In this article, we would like to focus on three areas where EHR analytics support patient centricity in clinical research. Firstly, EHR enables a move towards digitalization of trial systems and processes, allows trials to escape the confines of sites, and thereby makes it easier for patients to participate in decentralized, or virtual trials. Secondly, electronic systems democratize information, giving more information to patients, allowing them to make more informed decisions, thereby improving engagement. Thirdly, EHR analytics offers great improvements in efficiency of trial processes, from protocol optimization, to site selection, to patient recruitment, thereby ensuring the right patients are identified for the trials and accelerating the entire trial.

1. Decentralized Clinical Trials

The full promise of virtuality in trials lies in the idea that each participating patient may effectively participate in the trial at home, at their own convenience. In the USA, 70 percent of potential participants live more than 2 hours away from the nearest study center[6], which clearly creates a time/cost burden for multiple visits to a trial site and participation in the trial, such that less than 5% of the US population participates in clinical research[7].

In Decentralized Clinical Trials (DCTs) (also known as "virtual" trials, "direct-to-patient" trials, or "remote" trials), patient data is collected in the home or in the study participant's natural environment. A DCT trial does not require an intermediary like a study team or phlebotomist, but can rather be collected by the patient themselves, i.e. is "patient-generated."[8] This gives the patient control over and great flexibility in their participation in a clinical trial. Patients who have difficulties in mobility, e.g. the old and infirm, may now participate. Further electronic ("telemedicine") services enable patient recruitment, the obtainment of informed consent, measurement of clinical endpoints, and monitoring of adverse events from the patient's home, by the (remote) principal investigator and virtual care team.[9] DCTs are therefore fully patient-centric in facilitating participation in trials, reducing practical, financial and geographical barriers to participation and simplifying the patient journey.[7]

This, in turn, maximizes patient eligibility and supports enrolment, retention and compliance. DCTs are therefore also attractive to the trial sponsor, who benefits from not needing to compete for access to busy trial sites[10] and saving the costs of running full trial sites[11]. The benefits also accrue to the principle investigator: "DCTs can recruit more people into trials, increase retention and engagement, collect more continuous data in natural settings, while shortening the study time (faster to market), and decreasing costs."[8] "This model provides for better physician oversight and round-the-clock data collection… it reduces variability in assessments and data, and provides greater visibility into safety events."[9]

Clearly, this is all only made possible by technological advances which have produced wearable sensors for remote collection of data, systems and processes for remote consent ("eConsent"), electronic outcomes assessments(eCOAs), equipment and systems for home-testing (*e.g.* phlebotomy), cloud-based platforms for data collection, and automated shipping of drugs, all removing the need

for on-site visits to a physician's office or hospital.[8] Note: not every trial can work decentralized: if tests require expensive, specialized, equipment, then it makes more sense to run the trial at a site, or at least run a hybrid trial.

2. Democratized Engagement

All these electronic, digital, online systems are enabling a more balanced engagement between the patient and the study, evening out the asymmetry in the relationship until now. The patient gains resources which educate them on the full clinical trial process, risks entailed, and benefits to their situation; the patient gains oversight on which trials they may be eligible for and where they are; the patient makes an informed decision to participate in a trial.

There are (commercial) simple-to-use, direct-to-patient systems models which give patients and researchers a web-based platform on which to interact and communicate during the trial. Up-to-date information about a trial, or the trial process, can be distributed to all patients across all trial sites via document libraries and eLearning tools – allowing self-paced training – and their understanding of them can be monitored, effectively. The patient can have "pushed" to them step-by-step instructions for self-assessments, or reminders about their therapy schedule. This offers benefits in improving engagement and adherence. It empowers the patient with information to make informed choices and thereby more control over their own treatment.

Traditionally, it has been the task of a trial physician to realize that a specific patient matches the requirements of a clinical trial, and then to contact them to ask if they would like to participate in the trial. A second promise of EHR-based analytics is that the patient may automatically receive information about clinical trials to which they match eligibility criteria, which are being run in the hospital they are in, or nearby. This would give them a wider palette of treatment options to select from.

One advantage of electronically trackable interactions in a platform for distribution of information is that it provides an efficient infrastructure for training and consent. The patient's understanding of a study and the processes they undertake may be recorded by use of an online questionnaire. The patient's consent can likewise be registered by electronic consent ("eConsent"), which removes the risk of mishandled consent documents and subsequent issues in regulatory inspections. With the proviso that an eConsent system must adhere to local consent regulations (e.g. the US FDA's eConsent guidance document of Dec 2016), this automates and makes more efficient the process for patients making informed consent to participation in trials.

As with decentralized trials, the benefits of these three avenues of electronic patient engagement also accrue to trial investigators and sponsors, since they simplify processes and make them faster and more efficient, streamlining processes and reducing costs.

3. Accelerating Clinical Trials

Indeed, integration of EHR data allows acceleration of many clinical trials processes, simplifying the trial experience for patients and ensuring they get access to treatment options relevant to them. The benefits arise along the entire trial process, from the development of the trial protocol, to matching of trials to sites with enough matching patients, to matching patients to relevant trials, to acceleration of startup and running of trials, to greater patient adherence and retention during the trial.

Clinical research studies are becoming increasingly complex, with studies that may have challenging inclusion/exclusion criteria, urgent timelines or other studies competing for the same facilities. Patient recruitment is perhaps the biggest challenge to the success of clinical trials. Approximately 80% of trials fail to meet enrollment timelines and 30% of Phase III study terminations are due to enrollment difficulties.[12] One study of almost 8,000 cancer trials found that 20% failed to complete: a waste, not only in terms of funding, but also the time and commitment of the 48,000 patients involved.[13]

The key reasons for recruitment delays are the uncertainty of estimating the number of patients at sites, and the resulting difficulty of selecting sites that can actually deliver patients within the targeted recruitment time. Trial patient recruitment is often hamstrung by the so-called "Lasagna Law" which posits that "the number of patients predicted by investigators typically falls by up to 90% at the start of a study."[14] Other hurdles include revisions of the trial protocol (i.e. the list of requirements, often complex combinations of criteria, to select patients to be inducted into a trial) and the limited, competitive landscape of hospitals able to run trials.

The most effective means of mitigating the risk of study delay is conducting a comprehensive RWD-driven clinical trial feasibility assessment based on EHR data. From the patient's perspective, what's crucial here is that they can be found by the sponsor and that their treating hospital can be selected as a trial site. Site selection must be based solely on evidence that a site is expected to perform well. This includes evidence-based feasibility (Ebf) on all available data of a site's past performance and assessing the impact of its inclusion/exclusion criteria on anonymized real-time EHRs.

Using a large federated system and representative patient pool (Figure 5), EbF allows the identification of the proportion of the population that matches the protocol, and is able to demonstrate the potential impact on the availability of eligible patients if some of the inclusion/exclusion criteria are changed. Limiting the analysis to a country, or region, it also allows investigation of region-specific clinical practice/standard of care, patient pathways, referral networks, and potential recruitment rates and challenges. And drilling-down to site level, the same EbF can identify potential trial sites by showing which hospitals host the highest numbers of eligible patients for that protocol. Finally, with the right EHR coming from a global site network and technology infrastructure, eligible patients can be discovered which match the criteria of the protocol, and in real time.

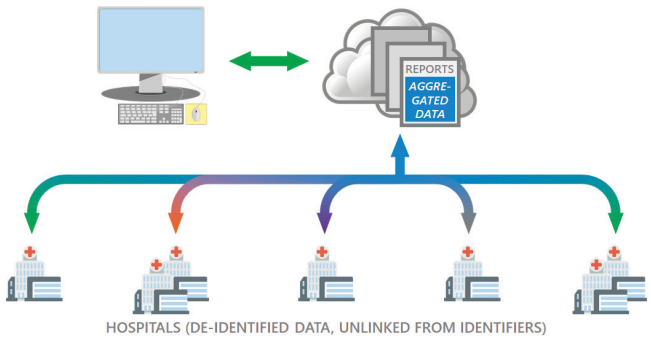

Figure 5: A federated network of hospitals queryable from the cloud, while maintaining patient data privacy and security by de-identifying the EHRs and keeping them within the IT infrastructure.

Use of EHR in EbF and recruitment processes clearly then enables patients to be better pre-screened and thereby experience faster screening and enrolment. They also enable trials to end on time (or earlier) due to faster completion of recruitment and, at the very least, offer a data-driven basis for performing risk-adjusted planning and scheduling.[15] Lastly, a patient who is well-matched to a trial will

have a higher likelihood to remain in the trial until the end, boosting retention. EHR data is improved by health professionals when recruitment and retention are based on electronic data.

Once past the recruitment stage, live access to EHR will also offer benefits for the efficiency of the running of the trial itself, enabling medical teams to act quickly and thereby shortening time to enrollment of studies.[11] Meanwhile, technologies for transfer of data from EHRs to the clinical trial management systems via electronic data capture are already available and lubricating the flow of information within a trial, allowing lossless data flow. Electronic Case Report Forms (eCRFs) may now be fed directly from sensors and biometric devices, making the patient experience effort-free.[17]

On an industry level, efforts to create standards and an interoperability infrastructure for electronic data sourcing (eSource) are being spearheaded by TransCelerate. Data types include data from devices and apps, EHR, data from other sources and directly entered data.[16] This topic has been given greater prominence by the US FDA's recent guidance on integration of EHR and EDC data in July 2018, which commits to "furthering the advancement and usage of new technologies in scientific and regulatory processes... [and] Modernize and streamline clinical investigations." As we have seen, such efforts will have great positive impact on the patient experience during clinical research.

Conclusion

Patient centricity puts the patient back at the heart of drug development, prioritizing the patient experience, needs and outcomes. Use of EHR offers a number of avenues which can support a patient-centric approach to clinical research, including removing barriers to participation via decentralized clinical trials and thereby supporting retention and adherence. Electronic information systems also create stronger patient engagement by simplifying and automating access to information, and enabling informed consent. Lastly, the patient recruitment processes are accelerated and made more efficient by use of EHR-based analytics.

"Since my diagnosis I have come to understand that people don't really understand me as a patient and what my challenges are." – David Ashford Jones: pharmaceutical executive turned patient advocate.[1]

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