

The Benefits of Patient Centricity in Clinical Trials: How it can Support Clinical Operations and Study Adherence

Patient centricity in clinical operations and study adherence is growing in popularity. A patient-centric approach means that the needs of patients are placed at the forefront of all decisions and actions within healthcare organisations. This includes all aspects of care, from research and development of new treatments to delivery of care. Patient centricity can be summed up by the phrase "the patient comes first."

There are many benefits to implementing a patient-centric approach in clinical trials. Patients feel more valued and respected when their needs are considered in all aspects of the clinical trial. This can lead to increased satisfaction and compliance, with fewer missed visits and improved data capture from off-site data capture devices like electronic patient reported outcomes (ePRO) diaries and other electronic devices. Wearable devices can continually capture patient data, but also involve the patient compliance and keeping the wearable device on. A patient-centric approach can improve clinical outcomes as more robust data is collected for the trial, in real-time with high quality data for analysis, but also it can improve patient recruitment as more flexible and easier trial designs can become less of a burden on patients and make it easier to attract and enrol patients into a clinical trial.

In a patient-centric approach to clinical development there several are emerging trends:

1. Decentralised Clinical Trials

Clinical trials have traditionally been conducted in centralised, highly controlled environments with the perceived benefits of increased efficiency and better data quality. Patient centricity is driving the need for decentralised and virtual trials as patient engagement and experience are key factors in the success of clinical trials.

The transition of clinical trials from investigator sites to subjects' homes promotes a more patient-centric approach while also reducing stress on clinical trial staff with

fewer subjects coming to site. It also opens many exciting possibilities for the collection of real-time data via wearable and other modern technologies.

2. Adaptive Trial Designs

Traditional clinical trials are designed with a fixed, predetermined endpoint. However, patient-centricity is promoting the need for adaptive trial designs. This simply means that an element of the study (e.g., sample size, treatment arms, population of interest) may change during the study if predefined and specific rules are triggered. This flexibility within the adaptive design framework can lead to improved use of available resources (e.g. by dropping an ineffective treatment arm) which results in reduced visits or smaller patient samples and less burden on subjects as they can finish a trial earlier.

We are seeing Bayesian adaptive designs being increasingly used in early phase development. These designs use data from the study as it is being generated to adapt the design on-the-fly. This can allow for more efficient trials by reducing patient exposure to ineffective treatments or by increasing enrolment in a trial that is proving efficacious. This can help identify optimised dosing for novel therapeutics.

3. Optimised Dosing

In oncology trials, we are seeing more patient-centric approaches with optimised dosing under the FDA's recent project Optimus. This project challenges the status quo in current oncology studies of finding the maximum tolerated dose (MTD) for the highest efficacy on clinical benefits to the cancerous cells. Instead, the trial design focuses on the efficacy of a wider range of doses and not the MTD which has the highest allowable toxicity to a subject.

This is a patient-centric approach because the impact of the trial drug on the patient's wellbeing is receiving greater attention. There are increased expectations on evaluating and performing additional research and analysis on the efficacy of smaller doses. These smaller doses are perhaps less toxic but may hold the desirable efficacy in relation to meeting the oncology-specific trial endpoints.

4. Personalised Medicine

Modern oncology therapeutics are increasingly becoming personalised medicines as patient populations are more frequently defined by their molecular characteristics, rather than the location of their tumour. This means that trial designs and patient recruitment strategies must be responsive to the unique needs of each individual patient.

One of the main benefits of personalised medicines is that they are tailored to each patient's specific genetic make-up. This means that the patient is more likely to respond to the treatment, as it is specifically designed for them. Personalised medicines have grown in popularity as the industry has the genetic markers to identify disease subtypes.

We are also seeing that drug combinations are increasingly being investigated. For example, a patient with a lung cancer might receive a combination of therapies, each of which targets different molecular pathways in the cancer.

Personalised medicines work best for a smaller population of patients who have a specific genetic makeup that is known to respond to that treatment or combination of treatments. This makes it more likely that the patient will respond positively to the medication and experience fewer adverse events.

Due to improved efficacy, we can expect reduced patient population sizes in trials. But as the definition of the disease is more specific, a challenge still exists for the pharmaceutical companies to recruit enough patients and those with specific disease enrolment criteria to the trial may be spread across the globe. Therefore, real-world data (RWD) can be used and the FDA's recent announcement on the ease of use of RWD will help drug makers with their patient recruitment. Patients can be enrolled from across the globe and they would not have to travel to site as data could be taken from their own homes. Also, there may be existing data within patient registries, medical records, and other databases available for analysis in the clinical trial.

These personalised medicines are often orphan drugs and can result in an expedited submission process and bigger treatment effects will be identified in a smaller patient population.

5. Quality of Life (QoL) Endpoints

We are seeing improved patient centricity with more trials including improved QoL in clinical development and a trial's endpoints. Not only is the drug efficacy analysed, but its impact on patient's quality of life is also going to be considered as a higher priority.

To make this a reality we need to see more patient involvement in disease specific questionnaires to help measure and report on this QoL, we also need to ensure compliance with the completion of these QoL questionnaires at home in the patient's own environment.

However, now, there are barriers in the adoption of these questionnaires, there is some stigma associated with the adoption of technology to capture questionnaire data from subjects. The industry can help the adoption of personal devices by explaining clearly to subjects enrolled in trials that by allowing a bring your own device (BYOD) will increase compliance and the probability of capturing data as it is all done from a single device.

There also needs to be a level of validation on the questionnaires to show that the responses are meaningful and related to the specific disease to demonstrate the validity of QoL endpoints. The design of studies to validate the questionnaires should involve patient groups.

6. Use of Technology to Communicate with Patients

Technology has made it easier for patients enrolled in a trial to bring their own devices. These devices can be configured to automatically send notifications to patients to complete questionnaires or diaries. In turn increasing compliance as data is more likely to be entered which improves the quality of these important patient-centric data.

Patient care and quality of life must be the focus, the use of technology to communicate and gather information has dramatically increased during the past two years and so now is the time to push patient-centricity further. The industry must come together to simplify processes as opposed to creating barriers.



Identification of key data is essential to patient adherence. It is not patient-centric to make subjects come to sites at an increased frequency to undergo many assessments. Improvements in design and data collection will enable the subjects to have an increased QoL and companies to streamline the analysis of data by capturing only the essential data.

Drug developers need to embrace technology to enable improved patient adherence and its especially important if RWD is being collected rather than from a designed study.

To make this a reality we are seeing:

- The increased user experience of mobile apps to help capture RWD.
- More education is needed on the use of Electronic Clinical Outcome Assessment (eCOA) data (which measures and records how a patient is feeling or functioning) and how it is

used and managed. Questionnaire data are still perceived as just additional external data which are expensive and time-consuming to setup. As an industry we need to see how we can make the adoption of innovative technologies easier such as wearable sensors. We should be opposed to the concept that patient-centric data is an expensive option, limited only to the richest of companies: biotechnology companies need to embrace a patient centric approach for the successful development of their pipeline of personalised medicines.

- An understanding on how we utilise the data from patient centric devices, we know the consistency between outputs from smart watches can differ by user, so we need to be clear from the start how we adopt and interrogate this data.

There are some barriers with the adoption of these latest technologies such as the validation of data that is required.

Traditionally, clinical trial data would be source verified onsite (unless done remotely) but RWE data that is collected outside of a controlled environment without a study nurse on-site does not have the level of source data validation a controlled trial has.

For RWE studies, the data that is entered is still checked against the source documents where possible such as prescription and/or any lab report/values and a copy of the source has to be saved for future audit purposes. There are certain remote source data verification tools that allows this with the use of scanning or taking screenshots of these source documents. However, this still does not cover the SDV of RWD from wearables and eCOA devices.

These devices focus on the most efficient and strict data transfer processing abilities possible, and are carefully validated so that data enters the database which will be analysed without any complications. However, due to the nature of there being no source documentation (think of a wearable on heart rate always providing real time data), the regulatory are still concerned

about SDV from these devices and the area is still debated today.

Conclusion

There are many benefits of patient centricity in clinical trials for both the patient, their families (when supporting patients with site visits etc) and the company conducting the trial. The patient needs are placed higher on the agenda of the trial which helps recruit patients and keep patients in the study, participating in a trial is easier and becomes less of a burden. This helps the drug developers as they will benefit from improved compliance and capture of data.

However, there are also some barriers to adoption that need to be considered when adopting patient-centric technologies, such as the validation of data from wearables and eCOA devices. There also needs to be an understanding from the industry how we move forward with the standardisation and adoption of eCOA and wearable data to ensure we can roll these offerings out to patients without the associated heavy start up times, therefore making them accessible to everyone and not just the companies that can afford the technology.

Pharmaceutical companies, Clinical Research Organisations, technology providers and regulatory agencies need to address these barriers and challenges and find solutions that still uphold the high standard of patient safety and drug efficacy but also now consider that patient centricity is no longer a trend, but a central tenant in many operations.



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