Real-world Data can Bridge the Gap Between Traditional Trials and a Patient-centric Future

Patient safety has been the primary focus of clinical trial design since 1947 when the Nuremberg Code outlined the ethical guidelines for clinical research. Consisting of ten points, those most directly relating to patients dictated that trials must be designed to avoid all unnecessary injury or suffering, that patients must give consent and are free to leave the trial at any point. The Code pervades all existing guidance and current world of drug development governed by ICH-GCP makes it mandatory to have all necessary steps taken by sponsors, CROs and investigators to keep patient safety as utmost priority.

The role of patients in pharmaceutical drug development then is fundamental. In the space of just 70 years the industry has moved well beyond patient consent and is beginning to embrace patient centricity. The benefits of integrating patient centricity into clinical trial design are far reaching, helping create better trials, better medicines and better patient treatment outcomes.

Benchmark data from across the industry indicates that on average across all protocol phases and therapeutic areas, sponsors need to identify circa 10 patients to randomise one, and roughly a fifth of those randomised will drop out.1 The question is then, how does the life science sector most effectively involve patients in the drug development process and clinical trials to improve experience and therefore, sign-up and retention?

Here, Karen Ooms at Quanticate seeks to answer this question.

Challenges to Patient Centricity

Randomised clinical trials have long been a central feature of the drug development process, giving us valuable information about the performance and safety of drug candidates. Nevertheless, they have shortcomings which prevent us from understanding the performance of new therapies and how patients experience treatment in the real world.

It is no surprise then that many pharmaceutical companies are looking for alternative sources of data to bridge the gap between traditional trial formats and patient-centric approaches. For a growing number of developers, real-world data (RWD) is essential to their solution.

Most pharmaceutical and biotech manufacturers believe that patient centricity will yield significant long-term, mutual benefits. The 2nd Annual Aurora Project's Global Patient-Centric Benchmark Survey1 canvassed 1,282 participants consisting of employees from across the sector, spreading across 113 countries. 85% of the respondents employed by the biopharmaceutical and medical device industries agreed the focusing on patients' needs leads to better business outcomes. However, they face many challenges to achieve their patient-centric mission. Only 3 in 10 of the participants were confident that they could deliver against patient-centric missions and just over a fifth believing that they know how to teach patient centricity to their employees.

So, what are these challenges?

Firstly, regulations affect sponsors' ability to connect patients' data across the ecosystem. Organisations must carefully balance managing patient data privacy with capturing and harnessing valuable data for optimal drug research and development. Regulations such as the Health Insurance Portability and Accountability Act (HIPAA), and the EU's General Data Protection Regulation (GDPR) can prevent researchers from understanding how individual trial participants interact, respond to and experience treatments.

These regulations are however essential as they ensure that personally identifiable information is never shared without permission. Currently, they also prevent data integration across multiple sources and researchers struggle to form patient treatment modalities that integrate with real-world evidence (RWE) to improve outcomes for specific patient populations.

Secondly, many companies are organised in silos around clinical, medical, and commercial structure, lacking a common function that connects patients from drug discovery to delivery and into pharmacovigilance and lifecycle management. This causes valuable information to disseminate and creates white spaces where knowledge is lost between departments as the therapy progresses towards commercialisation. This absence of a patient-focused function across a product's lifecycle often impedes patient-first thinking, especially where functions lack clarity on overlapping responsibilities for patient care.

Finally, at the clinical stage, trial data alone is not enough to develop a truly holistic understanding of the effectiveness of a new drug product:

- **Difficulty ensuring adequate representation** – finding enough patients to ensure adequate representation of all those who can benefit from a drug candidate is a common challenge. This becomes magnified in studies of treatments for rare diseases, or for demographics where there are ethical concerns, such as children, pregnant people or groups where there are more likely to be comorbidities (usually the elderly).
- **Narrow inclusion criteria** – the exclusion criteria in many studies will focus on patients with comorbidities and organ dysfunctions, who are under concomitant treatments or who are over a certain age limit. In the real world however no such limitations would be in place and the patients taking the drug could be elderly or have other conditions requiring treatment. While the intention is to reduce confounding factors to gather information applicable to the average patient, it means that developers don't have a complete view of how the drug is working, how it may interact with other treatments and how it could affect other diseases.
- **Poor patient adherence** – during trials, participants are often more compliant with instructions and will have greater access to support and more regular interaction with medical professionals.

At home, however, patients take and manage their medications very differently – they may take their dose at different times of the day, or they may forget to take it altogether. They may even struggle when self-administering, leading to uneven dosage quantities.

- **Different perspectives –** varying perceptions of what constitutes a meaningful impact on symptoms and quality of life among both healthcare professionals (HCPs) and patients is something that cannot be accounted for through clinical trials alone.

Engaging People, Not Patients

Becoming more patient centric in clinical trials starts by engaging patients more as individuals. If research partners can design studies focusing on outcome measures that are meaningful to an individual patient, this is a move towards becoming more patient centric.

To address the challenges above and work towards patient centricity, trial designers are increasingly:

- **Selecting endpoints that are meaningful to the patients and easily understood.** These might be characterised by levels of tiredness or pain and can be used alongside the traditional measures of symptoms or disease progression.
- **Designing the study with the patient experience in mind.** The number of clinical visits and the time of day and clinic location all impact the patient experience. Complicated treatment regimens can diminish willing participation and jeopardise data quality.
- **Providing a report written with the patient, not the clinician in mind.** 'Plain Language Summaries' written in addition to clinical study reports help patients understand the results of a study and improve their perception and experience of it. These are currently not mandatory but there some discussion and expectation that they will become a regulatory requirement.
- **Taking advantage of the cloud to communicate and monitor patients remotely.** With the advent of smart phones, wearables and applications, it is possible to collect more actionable data in real time.

Mining Rich Trial Data for Patient Truth

To assess what is happening in the real world, rather than just using clinical trials to collect data, researchers are looking to use data which has come directly from the market – RWD – to provide RWE for their treatments.

The US Food and Drug Administration (FDA) defines RWE as "data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials".

This RWD includes electronic health record data, insurance claims, device data and other patient-generated information. It also includes genuine ongoing conversations between doctors and their patients about genuine day-to-day experiences of their conditions, and of their treatment.

Such data can be collated from a wide range of sources, from medical databases kept by state healthcare systems or private HCPs to records of health insurance claims held by medical insurers. Patient-generated data from wearables or medical devices used at home can also be harnessed to generate real insight into how patients respond to treatments.

Biometric experts have much greater latitude in collecting trial data. Real-time electronic patient-reported outcomes offer researchers new ways to assure patient safety and the clinical assessment of the candidate. Advances in artificial intelligence and machine learning are also helping trial designers reach out to patients and connect them to the right clinical trials.

The integration of mobile health (mHealth) tools can generate large streams of data that researchers can explore, analyse and draw conclusions from. By creating a rich data-centric environment, researchers have a more accurate picture of the patients' reality, avoiding having to rely on patient recall, and possible bias to the data caused by inaccurate recall, or influences of patient perception.

Why RWD is Coming of Age

The 21st Century Cures Act in the US and the Adaptive Pathways approach from European Medicines Agency (EMA) both evidence that regulators are placing more emphasis on patient focused drug development. And there is further precedence – the FDA approved Pfizer's Ibrance treatment in 2019 using analysis based largely on RWD – a first for the pharmaceutical industry.[2] The COVID-19 pandemic and the race to develop vaccines have also served to highlight the genuine positive impact of RWD on pharmaceutical innovation. CROs have seen demand increase for real-time evidence of treatment performance in patients hospitalised with serious cases of COVID-19, as well as information about the longer-term efficacy of the vaccines already introduced in the market

Through an anecdotal lens, observational longitudinal databases of RWD allow for in-depth analysis by experts. These databases contain de-identified medical records for many patients – one of the largest with contains information on more than 100 million patients – over the course of several years. This is a much larger scale than regularly used in clinical trials.

Such a wealth of long-term information allows for analyses of rare diseases, treatment pattern changes and other factors, such as treatment performance alongside therapies for other conditions.

However, unlike in clinical trials, the researcher will not be able to randomly assign patients to a given therapy nor collect all characteristics that may be of interest. This is one reason why RWE should act as a complement to clinical trial data.

With all of this in mind, RWD offers considerable value when used to complement clinical trial evidence to accurately measure the efficacy of new treatments.

Standardisation Remains a Challenge

RWD is still in its relative infancy and the approach to collection, synthesis and interpretation is far from being standardised. There are no global agreements yet on what and how much information is collected, how and where it is stored, and how it is analysed.

For example, on the one hand administrative healthcare databases designed to be sent to insurance companies for billing of private medical care are easy to study, because they are clean and consistent. However, the data they contain are limited only to what are needed by the insurance company, which restricts the information they can provide.

On the other, electronic medical records (EMR/EHR) databases are disorganised, inconsistent and incomplete, as their information is collated from patient records held by multiple facilities and sources. Nevertheless, they provide rich data that offers incredible insight into patients' behaviour and attributes, such as lung volume or pain scores, all of which may affect their response to a particular therapy.

Summary

RWD has exciting potential to truly enrich pharma's understanding of cutting-edge new treatments. Using it as a complement to the insight gleaned from clinical trials, sponsors can overcome the traditional limitations of clinical trials in the future and help deliver ever more effective treatments that genuinely improve patients' lives.

While regulators and the industry is making moves towards patient-centric, RWD-enabled trials – a lack of standardisation both in terms of data management and in approach remains a roadblock. Customised, case-by-case approaches to analysing RWD effectively will be required for the foreseeable to ensure the full potential of data and therapies are realised. In the longer term, expertise in capturing, collating and studying RWD is crucial if pharmaceutical companies want to make sure they harness this new source of evidence to its full potential.

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