The Journey from Hesitancy to a Reliance on Real World Data

Karen Ooms, Head of Statistics at Quanticate explores the rise in the use of real world evidence (RWE) in the pharmaceutical industry in recent years, and argues that the concept of harnessing data from real-life patients has finally come of age.

As recently as just a few years ago, drug developers across the globe were hesitant of using RWE when pre-forming the clinical analysis of an investigator product. The gold standard of investigative analysis to determine the efficacy and safety of a new investigational drug remained the randomised clinical trial.

However, many statistical consultants have for a long time argued the merit of using real world data (RWD) to help create more efficient trial designs and provide, potentially, even more reliable data to inform clinical trials.

The debate is ongoing. However, the COVID-19 pandemic has forced a new-found reliance on RWD. Sponsors and their CRO partners are seriously considering harnessing RWD to help the world overcome COVID variants and ensure new vaccinations for these variants get to market quickly and safely in the continuing fight against the global pandemic.

With this in mind, has the use of RWD and RWE finally come of age?

The drawbacks of clinical trials

While randomised clinical trials are a crucial feature of any drug development process, providing valuable information about both the performance and safety of an innovative drug candidate, they do present drawbacks. These limit their utility with regards to developing a full understanding of the real-life performance of new therapies.

For instance, they have narrow inclusion criteria, which often means that patients under concomitant treatments, with comorbidities or organ dysfunctions, or over a certain age limit are left out of studies. This is designed to reduce confounding factors and to produce data that is applicable to the average patient. However, in the real world, many of the patients taking the therapy will have other conditions that require treatment with other medications. Not including these means that it is impossible to gain a full picture of how the treatment will work.

Further complicating matters is the issue of finding enough patients for the study to ensure adequate representation of all the possible patients who will benefit from the drug candidate. This is a particular problem for treatments for rare diseases, or for demographics such as children, older people, or pregnant women due to ethical concerns.

Actual patient adherence to the therapy is another factor that clinical trials cannot take into account on their own. During trials, participants tend to be more compliant with instructions. However, patients at home may take and manage their medications quite 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 – such as failing to inject or inhale an entire dose, leading to uneven dosage quantities.

Varying perceptions of what constitutes a meaningful impact on symptoms and quality of life among both healthcare professionals (HCPs) and patients is also not typically addressed through clinical trials.

With all of this in mind, clinical trials leave significant gaps in our understanding of the true performance of new treatments. During the COVID-19 pandemic, with the need to access data rapidly about the efficacy of treatments for patients hospitalised by the disease, the need to fill these gaps became particularly acute. It is no surprise that more and more drug developers took to exploring RWE as a means of addressing this issue.

Explaining RWE

To assess what is happening in the real world, rather than using clinical trials to collect data, the researcher may 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".[1]

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 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.

The benefits of RWD

Observational longitudinal databases of RWD allow for in-depth analysis by expert clinical research organisations (CROs). These databases contain de-identified medical records for many patients – the largest one Quanticate works with contains information about more than 100 million patients – over a period of at least a few 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.

In addition, the de-identification process of these data needs to follow country specific guidelines for protecting individual health care information.[2] This means the available data does not include any information that could potentially be used to identify a person.

RWE is quickly demonstrating its value to the pharmaceutical industry and proving that it can be used alongside clinical trials to measure the efficacy of new treatments. For example, in 2019, the first drug was approved by the FDA – Pfizer's Ibrance – using analysis largely based on RWD.[3] Previously, drugs were approved based on data derived entirely or almost entirely on traditional clinical trials.

RWE in the age of COVID-19

The COVID-19 pandemic has provided an ideal scenario to highlight the genuine positive impact of RWE on pharmaceutical innovation.

A number of CROs have seen demand increase significantly over the past year for RWD from drug companies working on treatments and vaccines for COVID-19. This includes demand for evidence of treatment performance in patients hospitalised with serious cases of COVID-19, to information about the long-term efficacy of the vaccines already introduced in the market.

RWD can provide pharma companies with a wealth of information that can inform the search for improved therapies for in-patients with respiratory complications, as well as potential treatments for long-COVID symptoms. As more data becomes available, we can expect further innovation to be fuelled, benefiting COVID sufferers in the future.

Most importantly, RWD has the potential to provide life sciences professionals with rich data about the impact of existing vaccines on new variants as and when they arise. Armed with this information, they can pinpoint which variants pose the highest threat to public health, which variants require boosters, and exactly where and when intervention is needed.

As a result of all this comprehensive real-world information, pharmaceutical companies will be able to play an even more effective role in helping us to live with COVID-19 in the future. We will hopefully be able to save thousands of lives and turn the disease from disruptive pandemic into a manageable seasonal issue, as with influenza. The use of RWE in the pandemic even holds lessons for pharmaceutical companies focusing on the treatment of chronic or rare diseases, as well as cancer.

The future of RWE

RWD and RWE offers tremendous potential for improving our understanding of the effectiveness of the treatments we offer. However, the use of RWD is still in its infancy for the simple reason that the data itself – what and how much is collected, how and where it is stored, and how it is analysed – is a long way from being standardised.

Efforts are being made to counteract this, but they consistently sacrifice some database specific advantages. But it does mean each database has its own structure, advantages and limitations.

For instance, administrative healthcare databases compiled by medical facilities to be sent to insurance companies for billing of private medical care are clean, consistent and standardised, making them easy to study. However, they are restricted in terms of the information they offer, as they are limited only to data required by the insurance company.

Electronic medical records (EMR/EHR) databases, on the other hand, contain patients' medical records drawn together for multiple facilities or across networks all collated by one entity. Consequently, they are disorganised and difficult to compile into a single comprehensible database. Different approaches to define certain health events may be used by each originating database. Records may also be incomplete. However, the data they offer provides incredible insight into the unique attributes of patients, such as lung volume or pain scores, which may impact on their response to treatments.

With this complexity in mind, an individual, customised approach is vital when it comes to analysis of RWE. Working closely with an expert CRO with experience capturing and analysing RWD is vital if pharmaceutical companies want to ensure they get the most out of this new source of information and evidence.

Time to harness the power of RWE

While randomised clinical trials will always have a crucial part to play in any drug development project, we can expect RWE to have a far more important role in the future.

Such rich data, gathered in the field, over the long term and from a far wider selection of patients, offers an exciting opportunity to advance our knowledge of treatment efficacy. It also provides us with the chance to circumvent the limitations of clinical trials when studying rare diseases, helping us to deliver therapies and orphan drugs successfully.

Harnessing RWE effectively is complex and challenging. However, with expert support, pharmaceutical companies can ensure they make the most out of this rich new source of information, so they can go even further towards transforming patients' lives for the better.

REFERENCES

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