Review Article

Real World Evidence: An Overview of its Importance in the Current Scenario

Asraf Ali*, Anto Vijay Kanth, Rituraj Mohanty, Arun Gowda, Anand Patil
Focus Scientific Research Centre (FSRC), #19 KMJ Ascend, 1st Cross, 17th C Main, 5th Block, Koramangala, Bangalore, Karnataka, India.
***Corresponding author's E-mail:** asraf.ali@fs-researchcenter.com

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ABSTRACT

Real world evidence (RWE) studies generate convincing observational data outside of randomised controlled trials (RCT) to create more awareness on diseases, products, and patient populations. Since RWE can answer questions unaddressed by RCTs, it permits a universal assessment of a drug in a real world context and paves the way to better health outcomes and cost-effectiveness of new health technologies. Despite challenges and barriers that influence access to and the use of RWE data, stakeholders realise that observational studies that are properly designed and conducted can discover unseen facets of diseases that can help them take strategic decisions and deliver better health care. The need of the hour is a change in policy to negate the challenges and barriers in accessing RWE data, facilitating the utilization of the existing goldmine of data in the form of real world information.

Keywords: Real world evidence, Randomised clinical trials, Real world data, Health technology assessment.

INTRODUCTION

RWE is defined as data used for clinical, coverage, and payment decision-making that are not collected in conventional RCTs. It encompasses data from existing secondary sources (e.g. databases of national health services) to new data collected, either retrospectively and/or prospectively. It is a form of late-phase research studies - an emerging segment for patient centered outcome research[1]. The main goal of the pharmaceutical industry is to bring drugs and devices to market more rapidly to improve health outcomes for patients. RWE delivers a deeper insight into how a drug is actually utilized and attains fulfillment in the real world[2]. It plays a significant role in evaluating the cost-efficiency of a drug in a real-world setting and measuring its impact on improving the quality of healthcare[3]. RWE uses observational data, and compelling data outside of controlled trials to generate awareness on diseases, products, and patient populations[4].

DISCUSSION

The Importance of Real World Evidence

Randomised controlled trials (RCTs) are the gold standard to create clinical data on efficacy and safety to support product registration and consequent prescribing. Of late, analysts and academics have discussed the promise of real-world data (RWD), nodding at its potential to contribute to better health outcomes[5].

RWE is the "data collected in a real world setup for many purposes, sensible enough to demonstrate or negate a hypothesis that may have nothing to do with its primary scope"[6].

Several elements combine to make RWE vital and concrete. Payers are constantly under duress due to the sudden increases in the cost of drugs, all amidst limited healthcare budgets. New medicines cost a fortune and are not affordable many a times. Many of these medicines extend lives. However, the information from conventional trials are questionable, and it is difficult to figure out whether the drug companies are giving genuine worth in respect to their stratospheric costs.

RWE helps us define the subsets of patients who can most profit by a drug, in light of their hereditary qualities, social factors and disease variations. It also helps to choose where the most squeezing therapeutic needs are and support pharmaceutical companies to suspend drugs that do not adequately conform to the existing treatments. It additionally ensures that there are "safety signals" much faster, thus cautioning drug companies and the general population on the perilous reactions of certain medicines[7].

The attainment of a RWE study relies partly on real-world data as the most appropriate choice to meet the required objective. They can be a supporting factor by drawing the variances between actual and expected efficacy and safety in a real clinical setting. The launch of new drugs always comes with an uncertainty. RWE can decrease the uncertainty factor by a large margin with more information on the risks and benefits associated with a new drug to be launched[8]. RWE offers chances to decide new molecules, to line up resource development and support the molecule development decision making[9]. RWE brings many positives in its wake, be it on its own or in conjunction with clinical trials. The demand for RWE is increasing and is unlikely to decrease as health care decision-makers become progressively mindful of what it offers. RWE satiates several essential needs including the generation of evidence to develop drugs. Sensing its immense potential and the increasing demand, sponsors

and CROs are prepping themselves, infrastructure and otherwise[10].

Who is utilizing RWE today?

- ***Clinical development teams:*** To outline clinical trials in light of actual treatment practices
- ***HEOR, Epidemiology and Drug safety researchers:*** To increase understanding about patient databases
- ***Market access teams:*** To educate payers and HTAs on a product's value
- ***Brand and franchise teams:*** To understand their markets, distinguish their products and enhance stakeholder engagement[11].

What is in it for Stakeholders?

- ***Payers:*** Payers must adjust the need to deliver better health outcomes and access to new advances with budgetary contemplations. Clinical trials made for regulatory purposes might be deficient to determine payer uncertainty.
- ***Researchers:*** Systems and tools to analyse RWE data have been progressively far-reaching and available to researchers. Analysts are presently ready to answer an expanding number of essential health services and policy questions without the cost, timeframe, and inconvenience of leading high-cost experimental studies.
- ***Industry:*** The industry sees RWE as an extra chance to exhibit the cost of medicines, for both the patient and the health system. It might likewise give new chances to the industry to work with payers to propel novel ways to deal with pricing and reimbursement[6].

The significance of RWE is expanding in terms of setting a drug for ideal pricing and reimbursement; providing validated long-term understandings for health care providers; showing value for money for payers; and empowering best care for patients. RWE can address queries unaddressed by RCTs and can allow for a more holistic assessment of a drug in a real world context[12].

RWE use in Health and Healthcare

RWE-based methodologies help drug and device companies throw light on what happens to patients through their entire treatment journey. Real world data supplies relevant information on: comorbidity profiles of target populations, possible causes of a disease of interest, and informed decisions on market access, new indications and related pipeline investments.

Also, they can give supporting evidence on the economic value of interventions to payers, patients and government health agencies[13].

Currently, RWE is utilized by companies to support decision-making during drug development (burden of disease, patient profiles, current therapies etc.), and in the regulatory environment. Most newly approved medicines have observational studies either imposed as a requirement of the marketing approval or as a constraint in the risk management plan. Most RWE studies are post-authorisation safety studies, including drug utilisation studies, carried out as per the tools and mandates prescribed by the EU pharmacovigilance legislation.

These most often include registries or established pharmacoepidemiological methods drawn from the secondary use of healthcare data. RWE is also used to measure the background incidence of adverse events to understand the observed vs. expected adverse reactions in the post-authorisation phase[14].

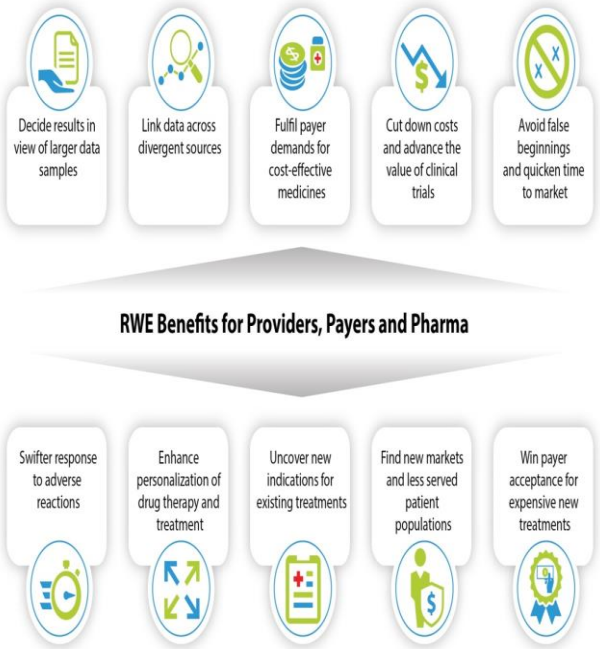

Figure 1: RWE Benefits for Providers, Payers and Pharma[15].

Perceived Challenges in RWE

RWE could play a major role in supporting bio-pharma companies in HTA submissions, predominantly in understanding the treatment pathway, connecting surrogate endpoints to patient outcomes, understanding heterogeneity and natural history of the disease, and eyeing the burden of illness and healthcare resource utilization in a real life clinical setting. The following are the challenges in the use of real world data;

- Timely collection
- Cost implications
- Managing missing data
- Bias in the data[12]
- Quality of data[16]

Patient protection and privacy are likewise challenges for RWE studies. Persisting data gaps suggest that the safeguard of patient privacy is inadequate, thereby posing

a threat to patient consent for RWE research, and public support and funding of research programs[17]. Legitimacy and unwavering quality of real world evidence is often hard to ascertain, and its sources are inadequately connected and incompatible in many cases[18].

Other Challenges include

- Lack of:
  - Standards
  - Knowledge in IT domain and utilisation of RWE between stakeholders
  - Electronic data collection and its consistency
  - Willingness by medical, nursing and other staff to adapt to change
  - Vendor support
- Debate on the investors
- Education and training of personnel on RWE
- Fear of technology failures
- Cost/benefit analysis

Factors that Influence Access to and use of RWE

There is a strong interest for RWE in the health and healthcare domain and researchers are utilizing it to address a range of issues.

However, research has also highlighted a series of barriers that may have an impact on the future use of technology and analytic capabilities and prevent researchers from exploiting the full potential of RWE[1].

- The rise of electronic formats to capture healthcare data has altered the cost, method and mode adopted by participants who generate evidence
- The ability to interpret RWE and apply it to key decision-making has accelerated
- Recognition that RWE has wide-ranging applications than research

Detailed RWE applications go beyond public evidence. But, the same techniques and data are used by pharmaceutical payers for internal business decision-making. Examples include designing trials, patient pathways and patient profiles or shaping the bond between key players[19].

Other Factors include

- Lack of shared standards on the content and quality of the data
- Methodological challenges
- Lack of shared standards on governance structures and privacy practices constitute significant concerns among most industries and public sector bodies engaging in RWE analytics[1].

RWE usage throws forth numerous challenges. Yet, data from clinical trials provide an accurate picture of the afflictions of patients. RWE data provide a better understanding of diseases and their occurring patterns, thus creating an ideal scenario for healthcare[3].

CONCLUSION

Real world evidence, apart from the known benefits to pharmaceutical companies of demonstrating value to the product, has been increasingly adopted to build awareness as well. Well-designed and conducted observational research can uncover hidden aspects of diseases that can help researchers and policy makers alike to be able to deliver care better. Researchers can better stratify and define patient segments, thereby ensuring that the right patients get the right access to care. Similarly, policymakers can unearth the potential of forecasting in an informed manner for the resource utilization needs for a particular disease or intervention. Challenges though persist in terms of conduct of these studies owing to associated questions around the quality of data and cost per patient. However, with the rise of technology and applications of sound designs and processes, these can be negated. What needs to be seen though is the time it takes for health authorities and payers to move out of the demanding for data outlook and set a change in policy to utilize the existing goldmine of data in the form of real world information.

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