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Unraveling the Potential of Real-World Studies

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Uttam Barick looks at the importance of real-world evidence, the current issues involving randomized clinical trials, and what questions should be asked when trying to determine the performance of a marketed product.

In the pharmaceutical industry, there exist fundamental variations between clinical trials and the real-life utilization of medicines [2]. Such variations create treatment and safety gaps which undermine the significant investments made by drug manufacturers.

When certain medicines are exposed to 'real-world settings' and experience safety issues and reduced effectiveness, this seriously limits the success of the marketed medicine, especially when compared to the results projected at the clinical trial stage. On top of this, the gap between what is estimated during clinical trials and the reality of a given drug usually necessitates an increase in resources.

Why is real-world evidence increasingly important?

In this modern, competitive healthcare marketplace, pharmaceutical and device companies are increasingly required to provide evidence on real world outcomes in order to differentiate, and justify, their products. In fact, in 2016, the US Food and Drug Administration (FDA) released a draft guidance document [3] on how real world data should be used when making both premarket and postmarket decisions for medical devices. This guidance has been created in order to develop a system that "would build on, and leverage, the vast amounts of data and information collected during the treatment and management of patients [4]".

Data generated from real world settings can help to provide significant insights into how a drug, or class of drugs, performs or is used in a real world setting. For this reason, it is important to continuously generate evidence-based information to attain optimum effectiveness and safety for the stakeholders involved.

The problem with randomized clinical trials and how they compare with real-world observational studies

Randomized clinical trials (RCTs), considered the "gold standard for clinical research [5]", are not without disadvantages and drawbacks. They offer proof of efficacy only under very controlled conditions. Normally, phase (I, II and III) studies represent a niche pocket of the population with specific characteristics, and therefore under-represent the greater patient populations. For this reason, RCTs might only be providing short-term outcomes.

It is for reasons such as these that some sources argue [6] large-scale observational trials might reflect the 'real clinical world' much better than an RCT performed in a specific, uniform subgroup of patients.

Late-phase and real world evidence studies demonstrate and help drug and device companies to understand the real picture of patients through the entire patient journey [7]. Since there are demands for ongoing investigations, therefore, it helps in generating and detecting the rarest safety signals by capturing data (structured and unstructured) from large populations and over prolonged periods of exposure.

Studies with a large number of patients from the real world setting have an advantage over trials conducted under controlled environments. Real-world studies provide the flexibility to monitor a number of parameters in order to determine the performance of a marketed product. Some of these parameters are:

- Will the product provide an equal, or greater, benefit when compared to other marketed drugs?
- Will the product be more cost-effective than the existing options?
- Will the product's safety profile be equal to, or better than, the alternatives in a real world setting?
- Does the product facilitate better compliance?
- Are there differences among individuals in terms of response rates?
- What are the differences in dosing and pharmacokinetic/pharmacodynamic [8] modeling?
- How does the product react in combination therapies?
- What changes are needed in treatment patterns?
- Does genomics play a role?

Late phase and real-world evidence studies have varied styles and designs, and Phase IV clinical studies are designed to get information from the real world setting to assess the treatment effectiveness for specific patient subgroups, or enriched populations, under the controlled protocol.

Patient databases, chart audit/reviews and registries expedite access to retrospective studies with sizable amounts of patients and data. These studies are ideal for the validation or generation of hypotheses for future studies, thereby feeding into research and development plans. The correct style and approach depend on the target, the required outcomes and other limitations, like time and information.

In recent times, retrospective data has been a source to determine various patterns that are not visible in a controlled clinical study setting. The ability to determine the right patient populations for a particular drug in order to arrive at the best outcomes is an input that real world data always provides to research and development teams. Through big data and predictive modeling, the existing real world data determines:

- Patient personas for improved outcomes by determining:
    - Patients who demonstrate better outcomes
    - Patients who need support to be compliant
    - Existing beneficial programs/interventions
    - Co-morbidities that change treatment outcomes
    - Patients more likely to switch due to a lack of results
    - Most practical frequency and methods to monitor in chronic diseases
- Predictive analysis to determine:
    - Future disease burdens
    - Resource utilization
    - Planning resources
    - Funding requirements
    - Benefits of population-based programs for screening

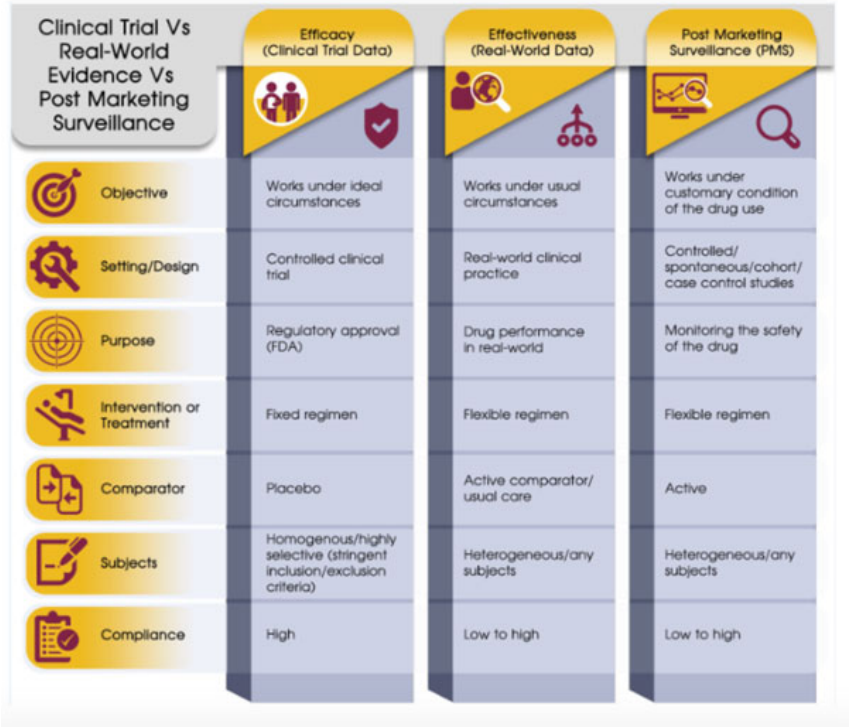
Given the importance of late phase and real-world evidence studies, and the potential implications of the results, it is clear that these studies should be designed and conducted with the identical scientific rigor we afford to randomized clinical trials. Though there are multiple operational barriers, which can be overcome with structured approaches, scientific rigor can increase the credibility within the scientific forum and with the policy makers.

The timing of late phase or real-world evidence studies are becoming increasingly important, as the market access [9] landscape continues evolving and adapting to the variations occurring in the healthcare landscape. Pharma and device companies are facing challenges during the post-launch phase in order to get a product to the right audience to influence greater adoption. These companies are taking the help of post-launch market studies, which hold the capacity to spawn insights from a wealth of information available from different channels. This is in order to help pharma companies unveil trends and patterns about patient adherence, switching, adoption, physician sentiments, KOLs, and sales force competency in a cost-effective way to create competitive advantage.

Life sciences, firms must concentrate on these studies and appraise them from time to time to attain business goals. “The more you know, the better for the patients” is the motto that must drive companies in order to attain the ultimate goal of patient benefit.

Sensing the same, the pharma world is experiencing a transformation. But, there is still some ground to cover which can be done with appropriate awareness by disseminating sensible information on these studies. The idea is to showcase the outcomes of these studies so that actual proof can encourage more companies to delve deeper and utilize the advantages of such studies.

Healthcare research and healthcare consulting firms have been striving to unearth the potential of such studies, and some stake claims to have dug deeper than many on the impacts and implications of such studies.



Conducting obvservational studies, both prospective and retrospective, enables us to uncover hidden gems in the form of real-world data. Using these studies, the diverse concerns of stakeholders, such as the generalization of results, healthcare professional interests, the quality of data collected, and the level of accuracy involved in such studies, can be anticipated.

Studies with a sound scientific design, standard operating procedures (SOPs) specific to real-world studies, creating owners among clinicians in publishing results derived from these studies, leveraging technology for remote monitoring, reducing time between reports by ensuring e-capture of data on intuitive systems with smart checks, etc. are a few ways to ensure the robustness of data.

Real-world studies are here to stay, and their usefulness and full-potential are only just being unraveled. There are various facets that are yet to be uncovered and tapped. The involvement of artificial intelligence [10] (AI) and Machine Learning in the drug development phase (a completely different topic that demands a separate write-up and discussion) has put us on the threshold of faster drug discovery cycles, reducing the importance of expensive and long-drawn phase trials. However, monitoring these interventions in the real world setting becomes more important as they need more intricate scrutiny.

Real-world data has always been around, but its significance has been not utilized to the full potential. However, the relatively easy access to it, technology interventions to capture quality data and make sensible decision out of them, AI and machine learning to look at data in novel ways and decipher more meaning from them, BIG-data capabilities to harness huge amounts of data over long durations of time and sift for quality information, and the economic sense of obtaining the desired results make it all the more interesting.

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Links:
[1] http://www.pharmexec.com/uttam-barick
[2] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf
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