Application of Real-World Research Method in Pharmacoeconomic Evaluation

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Abstract: As a response to solve the problem of medical resource allocation, pharmaceutical economics can direct drug pricing and other relevant medical strategy formulation. This study aims to explore how Real World can be applied in pharmaceutical economics research, applied to Real World Evidence as a basis for pharmaceutical economics evaluation, and improve the evaluation of the safety, efficacy and applicable value. Methods: Secondary literature study. Conclusion: The process of pharmaceutical economics evaluation based on real world research is summarized, which is conducive to improving the safety, effectiveness and application value of pharmaceutical economics evaluation, and providing ideas for making evidence-based health policy-making.

1. Introduction

As a special commodity different from other commodities, drugs play a vital role in the life and health of the people. They show particularity in both supply and demand as well as in the process of consumption. If problems occur in the supervision and administration of drugs, they will have a direct impact on the drug safety and life and health of the people. With the rapid development of medical science and information technology, people's demand for evidence-based health care decisions continue to rise, Real World Research due to better reflect the actual situation of characteristics gradually into people's horizons, Real World Evidence has become a health policy makers, practitioners, researchers and common focus of pharmaceutical enterprises. In the new medical insurance catalogue of China in 2017, the selection principle was changed from "safety, effectiveness and economy" to "safety, economy and effectiveness", and the "economy" was ranked before "effectiveness". It can be seen that the application of pharmaceutical economics has attracted more and more attention from relevant government departments, and the research results have become an important basis for the decision-making of administrative departments at all levels.

2. Pharmaceutical Economics

Pharmaceutical economics is a complex and interdisciplinary discipline, whose original intention is to promote rational drug use, control medical costs and reduce drug expenditures, make more efficient and safe use of medical and health resources, and ultimately improve the allocation and utilization efficiency of scarce and special medical and health resources. From the point of view of narrow sense, pharmaceutical economics is the application of cost-benefit analysis method of modern economics, economics, epidemiology, and with the use of decision science, clinical medicine, biostatistics, such as research methods, a comprehensive identification, measurement, analysis and comparison between the treatment strategies of different medicine, drug treatment with other intervention plans, and between different medical service project cost and output, evaluation of economic value of the difference between the different solutions, and to improve the efficiency of resource allocation and utilization of effective drugs by, under the condition of limited maximum limit satisfy the drug availability and use. From a broad perspective, pharmaceutical economics is a discipline that applies economics and other relevant knowledge to study the economic rules of drug resource utilization in the field of medicine, study methods and measures to improve the allocation and utilization efficiency of medical resources, and achieve the maximum improvement of health status with limited drug resources. At present, pharmaceutical economics is widely used in drug

catalogue formulation, drug price management, new drug research and development, hospital pharmacy and other aspects and fields.

3. Real World Study

The objective, data-oriented world without human interference is the closest to the REAL world. As a research method that has only entered the vision of Chinese medical and health researchers in recent years, Real World Research must clarify its relevant concepts before carrying out research. There are obvious connections and differences between the three confusing concepts of Real-World Data, Real World Evidence and Real-World Research.

For now, the concept of Real-World Data varies from one organization to another, but it is essentially the same. In general, we refer to Real World Date (RWD) from the real medical institutions, families or community environment rather than from scientific research sites with many strict restrictions. RWD can reflect the actual treatment process and Real health status of patients. There are also institutions and organizations that define real-world data as data other than traditional clinical trials.

Real World Study on the basis of the existing medical research evidence to establish scientific and effective health care policy is known as evidence-based medicine health decisions, and the key is valid medical research objective evidence. But a lot of raw Real-World Data is not the same as Real World Evidence, and must be transformed through well-designed real-world research. Real World Study (RWS) refers to a research method centering on relevant scientific issues, based on Real World Data derived from real medical environment, and integrating multiple data resources through comprehensive application of multidisciplinary technical methods such as clinical medicine, epidemiology, medical statistics, evidence-based medicine and pharmaceutical economics. The Real-World Study mentioned in this paper centers on specific medical policy issues the research method of pharmaceutical economics to transform Real World Data into Real World Evidence, so as to make evidence-based medical and health decisions on medical issues. This process of applying the results of Real-World Study to clinical and medical decisions is Real World Evidence (RWE). The essential difference between Real World Evidence and other evidence lies not in research methods and experimental design, but in the environment in which data are obtained, not in many strictly restricted scientific research sites, but in the real medical environment, families and communities. Real World Study can be applied to different clinical research issues, such as disease burden investigation, treatment model and utilization analysis, patient prognosis and risk prediction, etc. High-quality Real-World Study can play an important role in the evaluation and selection of different intervention plans in pharmaceutical economics.

Figure 1. Relationship between RWD/RWS/RWE

4. Application of Real-World Study in Pharmaceutical Economics

At present, China's medical reform and drug correction are at a critical moment, and the contradiction between the increasing medical expenditure and the unsatisfied medical service demand needs to be solved urgently. Rooted in the clinical practice in the real situation of the real world with high external validity, without strict set, easy to carry out research, the research results of authenticity guaranteed, collecting real reflect the reality of clinical data as the basis of

pharmaceutical economics research can make both efficacy and safety of medical evidence-based decisions.

The traditional Randomized Controlled trials (RCTS), which are widely accepted as the gold standard for clinical studies and pharmaceutical economics evaluation, can minimize possible biases in clinical trials, balance the confounding factors, and improve the effectiveness and safety of statistical tests. However, they also have the characteristics of "high selective population", "high cost", "high internal consistency", and "three high and three small", namely, "short study time", "small sample size", and "small representative in the real world". Therefore, the internal authenticity of RCT research results is relatively high, while the external authenticity is relatively poor. Therefore, it is impossible to determine whether it can be generalized in real clinical practice. In addition, in the real clinical medical environment, there are often complex problems such as drug use for special population and combination drug use. However, traditional RCT is an ideal environment with strict setting in all aspects. Such strict setting is likely to be out of clinical practice and needs to be limited to include the characteristics of the population. Therefore, conclusions obtained from traditional RCT data analysis cannot be easily extrapolated, and external validity has certain limitations. In contrast, the Real-World Evidence can better reflect the real clinical medical environment, and the research results have a high external effect, which requires no strict experimental setting and is easy to carry out. The key to identifying Real World Data has nothing to do with randomness or intervention[1].

Pharmaceutical economics evaluation is the core content of the application of pharmaceutical economics. The main method is to evaluate the economy of alternative treatment and prevention of diseases. The main purpose is to study how to obtain a greater benefit at a certain cost, so as to optimize the allocation and efficient utilization of limited drug resources in the society and maximize the improvement of patients' health status. Its main content includes the identification, measurement and comparison of costs and benefits. According to different measurement forms of revenue, the main methods of pharmaceutical economics evaluation can be divided into Cost-benefit Analysis (CBA), Cost-effectiveness Analysis (CEA) and Cost-utility Analysis (CUA). When the benefits of alternative schemes are the same, the cost of alternative schemes is compared relatively simply, that is, Cost-minimum Analysis (CMA).

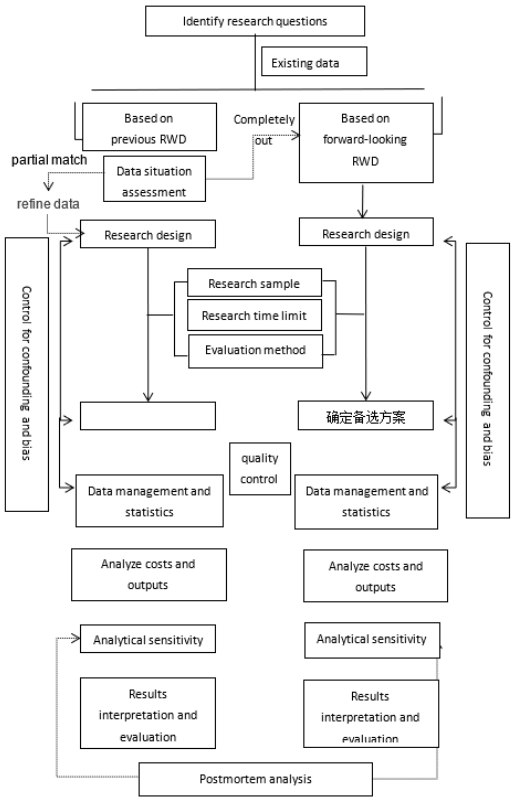

Figure 2. Process and thought of evaluating pharmaceutical economics based on RWS

Figure 2 shows the process and ideas of pharmaceutical economic evaluation based on Real World Study. In terms of research issues, the evaluation of pharmaceutical economic based on Real World Study can be used for the pricing of new drugs, market access, guidance of rational clinical use and screening of medical insurance drug catalogue. Research samples, used to carry out drug economics evaluation has a very wide range of Real World Data sources, along with personal electronic devices, the popularity of health-related applications, the establishment of various types of electronic databases, can obtain the Real World Data conditions increase, the study of the nature of the data also ensured the feasibility for the study of the real world, such as various agencies (such as hospitals, health departments, civil administration, public health departments) daily monitoring, recording, storage of all kinds of data related to health, the hospital electronic medical records, medical insurance claims database, public health and public health monitoring survey (such as the monitoring of adverse drug events), birth/death registration project, etc. When conducting research based on Real World Data, due to the high heterogeneity of population, the sample size required is generally large. In terms of study duration, the study duration of pharmaceutical economic evaluation was determined according to the nature of disease and endpoint indicators. Generally speaking, chronic disease or lifelong disease, endpoint indicators need a long time to be observed, the study period is long. In terms of evaluation methods, pharmaceutical economic evaluation mainly includes four evaluation methods: cost-effectiveness analysis, cost-effectiveness analysis, cost-benefit analysis and minimum cost analysis. In terms of data management and statistics, since most of the Real World Data are not generated under the principle of randomization, it is more important to use statistical test method when conducting pharmaceutical economic evaluation, and investigate the test effectiveness, so as to comprehensively control the risk of error in the inference and improve the reliability of the results. In terms of control of confounding and bias, when conducting pharmaceutical economic evaluation with real world data, there are many confounding factors, so it is generally necessary to identify the possible confounding factors based on existing studies, and then use statistical methods to eliminate the bias brought by these factors to the results. The commonly used statistical methods include stratification analysis, standardization rate, propensity score matching method, multiple regression model and so on. In terms of cost and benefit analysis, cost refers to the opportunity cost of resources or costs incurred in implementing a medical plan[2]. Cost can be divided into direct cost, indirect cost and hidden cost[3]. Direct cost refers to the direct cost of implementing medical plan, including direct medical cost and direct non-medical cost. Direct medical cost refers to the medical resources consumed in the process of treatment, such as drug cost, operation cost and so on. Direct non-medical cost refers to the resources other than medical resources that are directly consumed by patients in the process of treatment, such as transportation costs, accommodation costs, etc. Indirect cost refers to the loss of working time and productivity of patients and their families caused by treatment, such as wage loss caused by medical leave. The hidden cost refers to the physical and mental pain and discomfort caused by the treatment, such as pain, anxiety and tension. The form of benefit is measured and described in monetary form; The effect refers to the health effect of patients, and the effect of clinical diagnosis and treatment is used to measure the benefits (life year cure rate, effective rate, blood glucose concentration, cholesterol content, etc.). Quality-adjusted life years are often used to represent utility, essentially measuring the patient's psychological satisfaction. In terms of sensitivity analysis, the commonly used methods of sensitivity analysis include single-factor sensitivity analysis, multiple factor sensitivity analysis and probability sensitivity analysis. When the probabilities of different values of uncertain factors are the same, single-factor or multiple factor sensitivity analysis can be used. A single factor sensitivity analysis is an analysis that looks at the results of changing the value of one factor at a time. Multiple factor sensitivity analysis is to examine the results when the values of multiple factors change simultaneously.

In pharmaceutical economics evaluation method applied in the research of the real world, Real World Study is, in fact, many doctors based on the comprehensive research of many process vast amounts of data to the patient, can be seen as a continuation of clinical practice, in some sense better unified, the purpose of clinical research and clinical practice and research is not greater than the minimum risk. Therefore, it is of practical value and significance to further study and clarify the

ethics guidelines of traditional Chinese medicine in the real world and to guide the establishment of techniques and methods for the ethical review of real-world clinical research [4]. The main issues facing Real World Study in the ethical framework should apply the framework of systematic ethical principles of clinical research, including: social and scientific values, correct and fair selection of subjects, favorable risk-benefit ratio, independent review, informed consent, and respect for subjects [5]. It is ethical for clinical research to meet these conditions simultaneously. Ethical review of real-world research can consider the following principles and methods: Stratification to obtain informed consent; Strengthening information security and confidentiality; Layered privacy protection; Protect the safety of the subject; Strengthen personnel training.

5. Summary

The Real-World Data come from the actual medical environment, and the Real-World Data can better reflect the actual situation. The evaluation of pharmaceutical economics based on the Real-World Evidence can improve the safety, effectiveness, economy and applicable value of the evaluation. However, there are some limitations in Real World Data. In the process of using Real World Data to conduct research, in addition to considering the ethical issues of research and strictly checking the quality of data, some statistical methods should be used to eliminate confounding factors in the analysis process. Based on Real World Data it is important to note that research on the real world, in the process of research for observation the effect of patients with (such as observations may improve patient compliance, bring the placebo effect, etc.) or data loss from combining information errors, etc., also can make the results of the study can't absolutely on behalf of the actual situation, but just the opposite is true of traditional RCT can more close to reality. Therefore, when using real world data to carry out research, it is necessary to treat its advantages and disadvantages objectively, make use of its advantages and make up for its disadvantages, and give full play to the role of real-world data in scientific research.

References

[1] Sherman R E, Anderson S A, Dal Pan G J, et al. Real-World Evidence - What Is It and What Can It Tell Us? [J]. N Engl J Med, 2016,375(23):2293-2297.

[2] Sun lihua. Pharmaceutical economics [M]. China medical science and technology press, Beijing, 2010.

[3] Liu guo-en. Evaluation guide and introduction of pharmaceutical economics in China [M]. Beijing: science press, 2015.

[4] Wang sicheng, liu baoyan, xiong ningning, xie qi, zhang runshun, zhou xue-zhong, qiao jie. Ethical issues and strategies of real-world clinical research [J]. Chinese journal of integrated traditional and western medicine,2013,33(04):437-442.

[5] Hu jinhong, huang jin. Development status and prospect of medical research ethics [J]. Life science, 2012, 24(11): 1250-1257.