

Utilizing Patient Registries as Health Technology Assessment (HTA) tool

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ABSTRACT

Health Technology Assessments (HTAs) are gaining importance with support of governments in the Western World. With evidence synthesis and economic modeling gaining in accuracy and complexity, there is an increasing demand to assess the quality and validity of the data used for these studies. In keeping with the trend of the "Big Data" explosion, "Real World Evidence" is being seen as the answer to getting HTAs to the next level of accuracy. Hence there is the need for better tools to document and process "Real World Data". Registries have been existing for more than half a century now. However; their use was primarily done for epidemiological research. This article discusses how with the turn of the century, registries have evolved from being just portals for enrolment of patients to being highly sophisticated tools for economic modeling and cost analysis. We also discuss the challenges faced in optimal utilization of registries and how they can be addressed by better designing and implementation. We also discuss some policy decisions which have been taken to ensure that registries will continue to evolve and be a very important tool in HTAs.

Key words: Patient Registries, Health Technology Assessment (HTA), Comparative Effectiveness Research (CER), Real World Data, Evidence Based Medicine (EBM), Big Data.

SUMMARY

- "Real World Data" or Real World Evidence" generation is being considered as the latest trend in supporting HTAs in various countries.
- Disease registries, though existing since long, will now be utilized as a major platform for big data mining.
- Registries have the potential to influence healthcare policy decision making in time to come.

Abbreviations used: HTA: Health Technology Assessments, EBM: Evi-

dence Based Medicine, RWD: Real World Data, EHR: Electronic Health Record.

AUTHOR PROFILE



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BACKGROUND

Recession and financial uncertainties in the markets have made optimizing the use of healthcare and associated technologies imperative for governments in the Western World. Thus, Health Technology Assessments (HTA) are seen to be getting a thrust forward by the policy makers in United States and the United Kingdom, who rely on HTA for making their healthcare policies and budgets.¹

The importance given by governments to HTA to optimize the healthcare budgets is clear from the UK government's interest in setting up the National Institute for Clinical Excellence (NICE). NICE was set up in 1999, primarily as a premier institute for formulation of guidelines on management of diseases and new technologies. In 2005, NICE was renamed as National Institute for Health and Clinical Excellence (NICE) and entrusted with the additional work of economic evaluations. Today, it not only restricts itself to scientific knowledge and Evidence Based Medicine (EBM), but also conducts HTAs for therapies and pharmaceuticals. These are used by the government to assess the clinical efficacy of the treatments and technologies, and their cost burden to the National Health Services (NHS).²

Traditionally, the HTAs conducted depended on data generated by Randomized Controlled Trials and literature reviews on the subject. The RCTs are generally considered as "gold standard" in clinical efficacy studies. However, they are relatively short term studies, with a very well defined population, conducted within a controlled environment, with the sole aim of establishing clinical efficacy and safety. With time, the decision makers have realized that to come up with economic and coverage decisions, data from RCTs alone is not enough. It needs to be supplemented with data from the 'Real World'. That is, they need uncontrolled data from the general population, which would give a clearer idea as to what happens when treatment or technology is made available to the public at large. Thus with payers and policy makers, increasingly demanding knowledge of the economic and social implications (or The Real-World outcomes) from HTAs, it is no longer possible to restrict the data for HTAs to RCTs and literature reviews. Researchers are increasingly seeing the importance of getting a holistic view to their analysis by using Real World Data (RWD).³

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WHAT IS REAL WORLD DATA?

To put in simple words, the ISPOR Real World Task Force Report defines RWD as “data used for decision making that is not collected in conventional RCTs”.³ RWD comes from the confines of a natural environment. As such, it gives a better insight into the epidemiology of a disease, patient compliance and adherence to treatment and the costs involved; information which is more relevant to policy makers.⁴

Conventionally RCTs, the “gold standards” of efficacy studies are conducted in a well defined population, with specific inclusion and exclusion criteria, under almost “laboratory- like” conditions. Logically speaking, outcomes of RCTs cannot be extrapolated to the “Real World” in uncontrolled environments. Hence, it is clear that for predicting economic and social outcomes in the larger population, data from RCTs needs to be paired with data from the Real World.⁵

SOURCES OF REAL WORLD DATA

ISPOR (International Society of Pharmacoeconomics and Outcomes Research) identifies the following sources of RWD which can be used for HTAs.³ Each of these sources provides information to suit varying needs.

- Supplementary information collected during RCTs
- Large simple trials (also called practical clinical trials)
- Registries
- Administrative data
- Health surveys
- Electronic Health Records (EHRs) and Medical Chart Reviews

REGISTRIES AS SOURCES OF “REAL WORLD DATA”

Agency for Healthcare Research and Quality (AHRQ) defines a patient registry as ‘an organized system that uses observational study methods to collect uniform data (clinical and other), to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes.’⁶ In simple words, registries are comprehensive compilations of all cases of a particular disease or condition which happen in a given population.⁷ Typically registries store data for large number of patients, and follow up these patients over long periods of time, usually spanning a few decades.⁸

Registries were started back in 1930s in US and UK as means of systematically collecting data on cancer patients.⁹ In 1946, WHO started cancer registries worldwide with a standardized recording format, so that international cancer data could be uniformly collected. However, for a long time, registries remained only as sources of clinical and demographic data. They served to be of value primarily in epidemiology and research of cancer. Their value in conducting global research though, was recognized. In 1992, The International Agency for Research on Cancer collaborated with International Association of Cancer Registries to publish ‘Cancer Incidence in Five Continents’, with data from 140 registries worldwide.¹⁰

The use of registries in other fields of medicine and pharmacoeconomics however, remained unutilized. It is only towards the end of the last century that the number and types of registries being maintained started increasing.¹¹ With improvement in data collection and storage methods, the type and volume of data being registered also increased. In addition to incidence, prevalence and survival data, registries today have extended their scope to include clinical outcomes, drug effectiveness, outcome of treatments, compliance, QOL, and resource utilization data. Thus today, registries are seen to be capable of providing a wealth of information to

QOL analysis pharmacoeconomic research. Over the last decade the importance of registries in HTAs and coverage decisions is being realized.⁸ Registries can be classified based on the population defined by it.⁶

Some of the examples being:

Product registries-listing patients exposed to pharmaceutical drug or medical device

Health Services Registry-listing people undergoing a common procedure or clinical intervention or hospitalization

Disease or condition registries-listing patients with a common pathology.

Pregnancy registries-enlisting all women attending the antenatal clinics

A well developed registry generally integrates data from various sources. Primary data is collected for its defined purpose of listing. Secondary data is collected for purposes supplementary to, or not related to the registry. This data may not be as well structured or validated as the primary data. It is sourced from medical records systems, institutional or organizational databases, administrative and health insurance claims data, death and birth records, census databases, and related existing registry databases.⁶ Thus this secondary data is invaluable for epidemiological, social and economic research.

WHY REGISTRIES ARE IMPORTANT FOR HTA

Registries can be called as ‘storehouses of RWD’. Compared to all other sources of RWD, registries form a tool which can collate information from multiple sources. They can also be linked to other sources of RWD such as Electronic health records (EHRs) and administrative databases.⁶

Registries can be linked across nations, thus giving a perspective on changing trends across nations. This is of particular importance in cases of diseases common to a certain race or rare diseases.¹² The volume of data stored in registries is immense. Registries track data spanning decades, something which is beyond the scope of traditional RCTs. Patients are followed up in time after enrolling. Thus they give insights into changing trends of a particular disease, therapy and demography over time. Registries not only track clinical and drug related efficacy, but can also be developed so as to track economic data such as resource utilization and QOL. Thus they can be used for getting a holistic view from the data collected.⁸

The number of patients covered by registries is huge, unlike RCTs. The large number of patients makes statistical analyses and tests of significance more valid. Owing to the numbers involved there is also greater likelihood of detecting the relatively rare events which may be missed during RCTs. Though registries don’t have a control on the treatment given by a clinician, they can reveal the degree to which clinicians are managing a particular disease in accordance with the principles of evidence-based medicine. This information is of great use to healthcare administrators and planners, to get an idea as to how a drug or therapy is accepted in the Real World.⁸

Registries provide a detailed view of the morbidity, mortality and resource utilization associated with a particular disease entity. This data is of prime importance in coming to decisions on coverage of a drug or treatment. The collation of information is also quick and efficient owing to better methods of data management. Most modern databases are equipped with sophisticated data processing software and technologies.

REGISTRIES FOR PHARMACOECONOMIC ANALYSES

Registries are a source of clinical outcomes, admission and discharge, resource utilization and other data used for burden of illness, cost-utility and cost-effectiveness studies.⁸ Many cost analysis studies have been con-

ducted using registries in the fields of prostate cancer,¹³ radiotherapy,¹⁴ colorectal cancer,¹⁵ esophageal cancer,¹⁶ etc. using data from registries.

Evidence synthesis and economic modeling form an important part of HTA. Registry data has been used for economic modeling of colorectal carcinoma¹⁷ and decision analysis modeling of lung carcinoma.¹⁸ They have been used for preparing Markov models of arrhythmias¹⁹ and end stage renal disease.²⁰ Registry data has been utilized in cost utility studies by calculating the cost per QALY for cataract surgery²¹ and lung transplantation.²² There is a demand for prospective HTA of new technologies after coverage to make decision makers aware of the real world implications of the new technology. As per Varela-Lima et al, clinical registries are the most efficient tool for collection of such data.²³ Registries also gain importance in the evaluation of treatment of rare diseases and orphan drugs. Given the low prevalence of these diseases, it may not be possible to even conduct statistically significant RCTs. In these cases, registries give a larger pool of patients by bringing together patients from across the globe.¹²

Limitations of Registries

Even though registries seem like the “one stop solution” to all RWD capturing, certain limitations to the data capture process and validity of information have been highlighted.

The biggest limitation is the lack of established methodology and protocol for designing registries. Poor conceptualization and incorrect design can lead to misinterpretation of data or ineffective data.²⁴ If the definitions for data collection are not well defined at the time of building the registry, it may lead to highly suggestive, but incorrect data.⁸

The data collected by registries is not validated as compared to traditional RCTs. A lot of data is sourced from other administrative databases and records. Many a times there are gaps in the databases resulting in difficulties in processing the data. Due to lack of stringent validation techniques doubts may be raised regarding its value.⁶

Beside, as the data collected is non-randomized, there is a potential for bias.³ Registries have no control over the physician and the administration of treatment. Also there is no differentiation based on severity of illness amongst those registered. Physicians might try alternate treatments in the severely ill or non responders, which could result in skewed interpretation of the data.⁸

Need for better development of registries

Just as there is recognition of the immense wealth of RWD store in clinical registries, so also are researchers realizing damage caused by the flawed structure of a registry to the data. The Agency for Healthcare Research and Quality (AHRQ), which conducts HTAs for the US government, has prepared a dossier as guide to help healthcare organizations towards planning and implementation of clinical registries.

Some of the salient features of a registry to suit HTA involve ⁶

- A sound implementation plan- Feedback from Medical community and staff responsible for maintaining the registry is needed to estimate the sample size of registry, identify the cases and organize enrolment
- Well defined and documented inclusion/exclusion criteria and data sources
- Data collection protocol and appropriate tools to record data
- Data processing procedures and software
- Quality Control Procedures
- Data access policy
- Data and outcome dissemination network for optimum utilization of data

POLICY DECISIONS FAVORING REGISTRIES FOR HTA:

The need for including RWD complementary to RCT data in healthcare assessments is being realized across the developed nations. Since beginning of the century, many policy decisions have been taken up by governments indicate their commitment towards strengthening the evidence used for healthcare policy making. The US Centres for Medicare and Medicaid Services (CMS) released an updated guidance document on November 20, 2014 that describes coverage with evidence development (CED). The document validates the need for RWD and approves registries a source.

NICE which conducts HTAs for the NHS in UK, engages in synthetic modeling studies using RWD to predict real world effectiveness.³ The GetReal program by NICE, aims at improving efficiency of drug development using real world evidence. It is a public-private partnership represented by 29 partners including Health Technology Assessment (HTA) agencies and regulators, pharmaceutical companies, academia and patient organizations. The project began in October 2013 and is funded until 31 December 2016, by which time they aim to find ways in which RWD can help in pharmaceutical R&D and healthcare decision making.²⁵

REGISTRIES IN INDIA

While the developed world has realized the value of registries in epidemiology and research, India still lags in the number of registries and the information stored in them. Very few established registries exist such as the National Cancer Registry,²⁶ The Indian Transplant Registry²⁷ etc. The data contained is restricted to clinically relevant data with no insights into the economic implications of treatment.

In UK and US, the healthcare is funded by the respective government. As a result optimization of healthcare budgets becomes imperative for the government. Hence, HTA and recording of data to serve the needs of HTA becomes a necessity in the western world. In India, on the other hand, as healthcare is not funded by the government, it sees little incentive in assessing healthcare technologies and building systems to generate the relevant data. As a result registries, databases, medical records and other sources of RWD have remained undeveloped in our country. Hence, in India we are losing out on the tremendous wealth of RWD, which could have been generated, had our population been exposed to appropriate clinical registries.

The best source of RWD in the Indian context would be Electronic Health Records (EHRs). However, EHRs in India are fraught with many challenges.²⁸ Though the government has shown interest in EHRs, apart from a handful of premier institutes using them, they are yet to be accepted by the Indian Medical fraternity. Awareness, training and development of tools to capture RWD are the need of the hour for establishing a HTA system in India.²⁸ Unfortunately, while the developed nations are recognizing the value of HTAs and RWD, Indian government has shown no will to progress on this front.

CONCLUSION

In this era of “Big Data”, researchers world over are realizing the potential of Real World Data stored in clinical registries. With incentives from the US and UK governments, Real World Data could revolutionize HTAs, giving a better and holistic view of outcomes of new technologies. With advances, there is need to ensure that the potential behind clinical registries is unlocked and better registries and better data capture tools are developed.

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