ejpmr, 2016,3(5), 197-205

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

REAL WORLD EVIDENCE: A NOVEL STEP TOWARDS BETTER PATIENT CARE AND OUTCOMES

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Article Received on 25/02/2016 **Article Revised on 16/03/2016** **Article Accepted on 07/04/2016**

ABSTRACT

Role of evidence in continuous innovation and optimum patient healthcare is undisputable. This review attempts to provide a comprehensive view of "Real World Evidence" and its importance in current scenario. The various opportunities, challenges and applicability of the real world evidence in day-to-day clinical setup are captured here. Evidence validity and comparison with other established study design are also highlighted. Likewise, "Real World Evidence" should be harnessed further by marrying evidence, technology and regulation together for better patient outcome.

KEYWORD: Role of evidence in continuous innovation and optimum patient healthcare is undisputable.

INTRODUCTION

The global market for Pharmaceuticals/Devices is growing exponentially with companies expanding their reach in to newer geographic and therapeutic areas. Today as a result of globalization there is a simultaneous change in regulatory environment with increasing demands for product data or information at each stage of its lifecycle. Recent increase recalls and regulatory/legal settlements has led to regulators, policymakers/decision makers and end users requiring safety and efficacy data of medical products and including the detail information of the manufacturers. Pressure on healthcare budgets across the globe and demand for affordable and universal healthcare has added complexity to this scenario.

The usefulness of Real-World Evidence (RWE) has been debated and discussed for past several years. Analysts and researchers across globe have focused on its potential to contribute to improved health outcomes and better medical products.[1] Advances in technology help us to collect, analyze, share, and manage large data sets in real time at a relatively low cost. The increased use of modern technologies in the healthcare sector has changed the ways in which patient level data is collected, stored and managed.

There are currently approximately 500,000 different types of medical devices in the market, and the development of intelligent medical products (active implantable medical devices, networked medical devices etc.) represents a huge opportunity to collect large patient-level data in real time.[2] In this context, RWE can be used in conjunction with randomized controlled trials (RCTs) and other medical data to provide insights into real-world clinical outcomes. A spectrum of stakeholders in health care research, innovation and delivery hope that the combination of laboratory data and RWE can be used to help develop more targeted drugs/devices and to encourage better use of those drugs/devices by clinicians and patients. Data relating to patient experience in using drugs/device and to the contexts and settings in which these are used could potentially play an important role in the way these trials are designed and conducted and supplement the processes of registration and post-marketing benefit risk analysis.[3,4] In the context of the severe cost and productivity challenges experienced in recent years, the prospect of data and mechanisms that could improve efficiency at multiple levels of the health research ecosystem without the cost of clinical trials is the need of the hour.

Considering this, RWE a form of late-phase clinical studies is an emerging segment for clinical and outcome research. Healthcare providers and payers expect better outcomes & greater value than current standards of care from newer interventions and turn to real-world clinical evidence to help substantiate these claims. RWE uses observational data, taking information outside of

controlled trials to create insights on diseases, products, and patient outcomes.

Real-world evidence is becoming an increasingly integral element of healthcare decision-making as Healthcare Technology Assessment (HTA), reimbursement agencies and payers become more demanding in terms of the relevance of clinical evidence and effectiveness to the delivery of care in clinical practice.

RWE can provide insights into various aspects of the market access strategy, from choice of comparators in pivotal trials to development of economic models. Treatment pattern surveys among clinicians provide critical insight and understanding of current disease management, patient selection, treatment decision drivers, and relevant comparators in individual markets. Burden of illness and epidemiological studies provide critical insight into the impact of a disease and its treatment on patients and healthcare system, and provide a platform to understand the economic impact of potential changes in treatment. Resource utilization studies provide inputs into budget impact estimates and cost-effectiveness analyses that reflect real-world clinical practice.

What is Real world evidence?

RW evidence is a broad term. RW evidence has been defined by an International Task Force 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. However, a more positive and pragmatic definition is data/information which describing day to day happening in standard clinical health care practice. Thus, RW may include evidence/data from existing secondary sources (e.g. NHS databases; disease registries) and/or new data collection, both retrospectively and prospectively.

RW evidence includes data on (Table 1)

- Outcomes (clinical and patient-reported)
- Resource use (NHS, patient and societal)
- Treatment pathways
- Service models
- Patient preference/experience/compliance

RW evidence/data studies are also referred to as non-interventional or observational studies which are used inter-changeably. Certain studies are also termed audits or service evaluations. Most importantly, no treatment or test would be changed for a RW data project. RW projects can be comparative, considering 'which is best?' or descriptive, looking at 'what is happening?' and they can be undertaken either retrospectively or prospectively in a primary, secondary or tertiary care setting.[5]

Table 1: Examples of RWE

Area	Content
Resource use	Cost, contact with the health system, treatment
Health outcomes	Observational indicators, eg medical records, hospital statistics, insurance data
Patient behavior	Compliance with treatment, outcomes, preference (from reported data or social media)
Population health	Clinical data - both structured and unstructured content (e.g. dictations, medical history, labs, images)
	Events that can be linked to public health: weather, disease outbreaks, local events
	Physiological data from at-home monitors and bedside monitors and sensors
Sales, Marketing and distribution	Data from insurance claims and pharmacies, digital marketing data, sales and product data
Longitudinal patient Record	Medical history (diagnosis codes, physicians' notes images), pathology, diseases, drug information, environmental factors, product information, social media activities over time.
Consumer engagement and analytics	Blogs, chat rooms, Patient Communities
Health monitoring and intervention	Streaming data from Monitoring devices, Personal devices, apps

RCTs vs Real World Evidence

The question that is often asked is what the difference between RCTs is and RWE is. Usually standard RCT that aims to establish efficacy and safety are predefined for very limited outcome measures governed by rigid protocol. Such interventions are double blind, very often in an idealized setting using double dummy to help maintain blinding. Well-defined inclusion and exclusion criteria are in place. Patients after securing their consensus are monitored closely for >90% adherence, essential to minimize confounding factors to avoid compromising the primary outcome of the RCT. This

measure is of utmost importance as regulatory approval of the data may critically depend on this. However the careful patient selection for a RCT results in representing a few of them from a cluster, and extrapolation of this information to large population may not be always the correct answer. For example, the patients meeting common inclusion criteria in RCT for a respiratory study with asthma and COPD could be as low as 3%.[6] It then would be very difficult to extrapolate the data or study endpoint form this study into real life for reasons which may, include patient preference, lower adherence and comorbidities. Oppose to this, 'real-world' studies assess effectiveness in large heterogeneous populations, which include patients with comorbidities and co-medications. In real world settings patients follows routine standard of care, taking open-label treatment for a prolonged or specified period, with no additional interventions and no attempt to change adherence. An Electronic Patient health records usually help to obtain long-term outcome data. However, the effectiveness of research is most with a retrospective design, which is usually limited by its non-randomized nature, and therefore more robust study designs may be required.[7] The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) recommends prospective observational studies for clinical effectiveness research along with other types of clinical effectiveness research studies, including retrospective and prospective observational studies, and pragmatic Randamozied Clinical Trials (pRCTs). Here, pRCTs are defined as large prospective clinical studies in which patients are randomized to two or more interventions, and then followed up according to the investigating physicians' routine clinical practice.(9) pRCTs not only fills the gap left between RCTs and non-randomized observational studies but also simultaneously brings a good approximation of real-world practice. However, pRCTs can be expensive and difficult to implement as they require enrolment of a large population to maximize external validity. Another limitation could be likelihood of treatment switch over during the trial, which may reduce the value of randomization.[9] The Salford Lung Study is the first attempt to carry out a pRCT prior to registration of a new treatment.

RWE and BIG data

'Big data' has been defined as a 'term describing the storage and analysis of large and or complex data sets using a series of techniques including, but not limited to: NoSQL, MapReduce and machine learning'.[10] Big data resides in unstructured datasets. While life sciences and healthcare research generally approach research questions through known structured data, unstructured datasets could be increasingly used in the near future. These developments could bring RWE and big data even closer. However, as the two concepts may appear interchangeable, it is necessary to differentiate: the focus of the definition of RWE is on the methods through which it is created (i.e. outside the framework of a RCT), but that of big data is a more operational one, focusing on the characteristics of the data set and the analysis that it makes possible. An example of a big data application relevant for the pharmaceutical industry is that of the Strategic Intellectual Property Insight platform (SIIP) database.[11] This cloud-based database aggregates worldwide patent data and scientific literature, with more than 30 million documents and over 200 million annotated chemical compounds, enabling insight into complex chemical and biological patents. When the concepts are compared there is some overlap. Data from several of the RWE sources – for example from personal or bedside monitors or social media activity – may also be seen as constituting big data, as they present large, relatively unstructured datasets that need support from specific software and rely on machine learning to discern patterns. However, other data sources included in RWE analytics include data collected over relatively small and structured samples and sets that do not necessitate big data powered algorithms for efficient analysis.

Importance of real world Evidence

Critical stakeholders like physicians, patients, providers, payer's, policymakers, regulators and competitors have initiated real world evidence strategies in different geographies, to contain healthcare costs, which is an undebatable imperative of payers and governments. In large developed markets, payers and regulators are moving toward systematic reviews of RWE on in-market products to confirm product safety and comparative effectiveness versus current products. The more developed healthcare systems are using this data to determine pricing and reimbursement decisions. Notable recent advances by the public payers in the United States, France, and Germany are moving those markets toward the already established role of health technology assessors in the United Kingdom, Australia, and Sweden. Private payers in the United States are navigating carefully, initiating partnerships and joint studies with healthcare co.to "understand" product value, but those partnerships will very likely evolve into new standards for what is expected in the dossiers that accompany market access appeals.

eHealth infrastructures databases and RWE

The development of RWE generation, collection and analytics heavily relies on electronic systems and infrastructures. This has led to the term 'eHealth' – an umbrella term describing the use of such structures. According to Marconi (2002), the term 'eHealth' describes the 'application of Internet and other related technologies in the healthcare industry to improve the access, efficiency, effectiveness, and quality of clinical and business processes utilized by healthcare organizations, practitioners, patients, and consumers in an effort to improve the health status of patients.' eHealth comprises institutional structures, data architecture systems, competence centers and legal frameworks. Competencies of eHealth authorities cover a range of eHealth instruments, including ePrescriptions,

telehealth and patients' electronic health records (EHRs) systems.[12]

RWE can be found in various forms and the data is embedded in multiple sources. As a consequence their generation, analysis and sustainability rely on a broad range of stakeholders who own and curate the data or otherwise interact, compete or collaborate with each other. Ownership structures have the potential to define the setup of possible collaboration structures regarding data sharing and use. For example, a post-marketing study conducted by Franchi et al. (2013)[13] demonstrated that it is feasible to pool administrative and clinical data on epilepsy from different sources to ensure long-term follow-up of patients with the condition. Their study analyzed data from hospitals, prescription records from pharmacies, prescription records for diagnostic tests and other data collected for the national health system. In this instance, sharing and combining many previously compartmentalized data pools is likely to improve partner collaboration and partnership outcomes between different stakeholders within the healthcare ecosystem.[14] Further examples of data, data use and opportunities for data pooling are presented in Table 2.

Table 2: Areas for RWE use in health and healthcare

Use case	Descriptions of use case	RWE leveraged
LIFESCIENCES		
Drug Development	In an area traditionally dominated by randomised control trials, RWE analysis can be used to assess the efficacy of different medical treatment and inform drug development strategies.	Medical history, demographics, pathology, regulatory filings, product information.
Post-market studies	RWE analysis improves understanding of safety and effectiveness of drugs and devices once they are on the market. It uses large sets of post-market observational health data to gain insights into disease, products and patients populations, in areas such as health outcomes research, drug effectiveness and drug safety.	Outcome data (ie hospital (re-)admissions, mortality rates), adherence, monitoring device data, pharmacy data.
HEALTHCARE		
Healthcare service delivery	Decisions at the individual and system levels increasingly incorporate evidence from RWE analytics. RWE is used to support personalised decisions on treatment options and healthcare delivery strategies, building on healthcare coverage, quality and costs analysis.	Service utilisation data, treatment uptake rates, treatment outcomes, insurer data, diagnoses, treatment, cost data
Longitudinal patient record	The ability to enable a healthcare provider to pull information about a patient from multiple sources.	Medical records, imaging, lab results, drugs, treatment, service utilisation data, diagnoses.
CUSTOMER INSIGHTS		
Claims and premium analysis	Insurance companies collect and leverage RWE in a variety of ways. Some of the most relevant uses of data analytics for the insurance sector as a whole include risk management and the fight against fraud; and the these companies build on RWE to support payment decisions.	Insurer data, medical history, outcomes data, cost data
Customer insights	Increasing understanding about the customers requires the ability to analyse the customer' (healthcare provider, patient) needs with regards to health, treatment, education, finances and decision - making.	Sales data, marketing data, cost data.

RWE is useful for building the evidence base for development and post-market studies in the pharmaceutical and medical device sectors

RCTs have conventionally been preferred for product development in the healthcare industry. However, RWE can also be used to assess the efficacy and safety of different medical treatments. For example, a study evaluated the efficacy of drugs used to treat Chronic Obstructive Pulmonary Disease (COPD) and the relationship between these data and the results of clinical trials, using data from the Optimum Patient Care Research Database.[15] Another study, The European Cubicin Outcomes Registry and Experience project (EU-CORESM), is gaining access to a registry that gathers data from 118 institutions. The study considers the characteristics of the patient population and the relative efficacy of treatment for skin and soft tissue infections.[16] The findings will also be used by the

company for in-house research, going beyond the scope of the EU-CORESM study.

Analyzing the long-term outcomes of an intervention/drug/device is critical. An example of medium-scale project using a disease-specific database can be found in a study using data from 870 patients to assess long-term outcomes of transcatether aortic valve interventions (TAVIs) based on the UK TAVI registry, which has been set up to capture the outcomes of all such procedures executed in the UK .[17] The study, one of the first of its kind to concentrate on a mid-to long-term timeframe, monitored survival and mortality rates for the interventions at 30 days, 1 year and 2 years after the event. It found that while a substantive proportion of these high-risk patients were deceased within the first year, overall the survival rates were encouraging.

Post-market risk assessment is critical. RWE can be used to gain an in-depth understanding of specific issues, including the long-term effects of different treatment options on a specific patient group, such as those registered in a disease-specific registry. Studies have evaluated large national datasets to assess the impact of drugs or medical treatments. These included a Danish study that evaluated the net clinical benefit of new oral anticoagulants versus no treatment in a 'real world' atrial fibrillation (AF) population.[18] The study used a long-term database covering all Danish patients discharged with AF over ten years (between 1997 and 2008), looking at patients' clinical histories, including pharmacotherapy, and premorbid risk stratification scores for stroke/thromboembolism. The analysis was further facilitated by linking the existing dataset to the unique personal identifier and Danish biobanks in order to assess the effects of three drugs compared to usual treatment and inform healthcare decision making. Studies at the national level can, then, draw on databases linked across multiple identifiers and databases (depending on the maturity of the e-infrastructure of the individual countries).

There are also examples of cross-border initiatives offering added dimensions by including a cross-national set of patients. The studies building on the EU-ADR database for example used eight databases 5 in four European Countries (Denmark, Italy, Netherlands and the UK) where both clinical information and drug prescriptions are recorded for large-scale drug safety monitoring. The database contains information about 30 million patients. The studies looked at drug safety across a range of diseases including acute myocardial infarction; acute renal failure; anaphylactic shock; bullous eruption; and rhabdomyolysis.[19] A further example is supplied by the VAESCO6 project which has supported studies in the areas of vaccine safety surveillance. This study involved seven databases from European countries (Italy, Spain, Finland, UK, Sweden, Norway, Denmark and the Netherlands), covering at least 26.67 million patients.[20] Its aim was the development of vaccine safety and best practices, evaluation of strategies and new methods and to facilitate data collection through common aims and standards, and to provide information on vaccination safety.[21]

Improving healthcare service delivery by using RWE

Healthcare delivery decisions at the individual and policy levels increasingly integrate evidence from data analytics. RWE, in some cases is used to support individualized decisions on treatment options. These options are then customized to the patient's specific genotypic characteristics and outcome probabilities. In other scenarios, data are incorporated into studies investigating questions related to health services coverage, quality or costs with a view to developing national healthcare delivery strategies. RWE and big data analytics are synthesized for initiatives involving personalised medicine and which require treatment decisions to be based on the individual characteristics of the patient. These cases use large datasets on treatment outcomes. In the EuResist project, algorithms processing genotypic information across a multinational database are used with other genetic and response indicators in order to determine the best course of treatment for individuals with HIV infection. The initiative aims to develop a system capable of predicting how patients are likely to respond to a specific method of treatment and consequently recommend a certain treatment out of a portfolio of options. In pursuit of this aim, the project builds on databases of genotypic information, which are combined with data on drug resistance. RWE analytics are particularly useful in supporting innovative ways to improve and optimise healthcare delivery. One potential area for innovation is that of expanding the potential range of healthcare services by aggregating data for decision-support and supporting telemedicine, as illustrated by the strategy for home care implemented in Southern Denmark. In this case, the new system was set up with the aim of improving outcomes for chronically ill patients. The strategy includes linking data across healthcare databases to create a holistic view of each patient; but also creates a platform that can integrate data from home monitoring and telemedicine applications and offer access to different healthcare professionals that can use the data to support their decisions. Furthermore, the automation of processes supports trends toward process optimization and an efficient use of time, while the business intelligence and analysis potential of the linked database may offer commercial value to the region. In other cases RWE analytics has been leveraged to optimize current processes in healthcare delivery and limit associated costs, for instance by reducing the number of UK patients that have to be readmitted to hospital with Chronic Obstructive Pulmonary Disease (COPD) following their discharge. In this case, the computing assets of the NHS enabled the analysis of multiple types of standardised patient and treatment data. The analysis supported the optimization of the treatment process for patient outcomes and cost implications for hospitals. Studies assessing healthcare delivery also

include research investigating the evidence on the uptake of existing services and their delivery, for instance the effect of uptake of cardiac rehabilitation (CR) treatments on survival. RWE has also supported studies focusing on evaluating the quality of care. Franzke et al. (2009) collected data on patients with acne. This research allowed the capture of raw data and aspects of subjective patient experience and socioeconomic factors reported by patients with acne vulgaris. The data were then used to analyse the patients' trade-offs in choosing between doctor prescribed medication and the acquisition of medical products through self-medication.

RWE is also being used to inform decisions related to the burden of medical treatment costs. For example, the databases maintained in the Swedish national and Italian regional healthcare systems have been used to assess the burden of costs related to cardiac diseases or cancer.[22,23] Lothgren et al. (2013) have simulated cost implications per patient and examined the budget implications of different drugs used by patients with bone tumours. While the researchers could not directly access the relevant data, they triangulated available sources to estimate cost burden per patient and at the system level in Austria, Sweden and Switzerland. They thereby determined the drug with the lowest administration and collateral costs. Roggeri et al. (2013) used a set of Italian regional databases (administrative databases of seven local healthcare units located in four different regions: Veneto, Toscana, Abruzzo and Puglia), linked with socio-economic datasets to assess the direct healthcare costs and resource needs associated with acute coronary events. Included in the study was information on demographic characteristics, prescriptions of drugs reimbursed by the national health system, hospital discharge records, outpatient visits and diagnostic-therapeutic procedures.

Factors that influence access to and use of RWE

There is strong interest for RWE in the health and healthcare domain and researchers are using RWE to address a variety 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[24] and prevent researchers from exploiting the full potential of RWE. The lack of shared standards with regard to content and quality of the data, methodological challenges, and the lack of shared standards with regard to governance structures and privacy practices constitute significant concerns shared among most industries and public sector bodies engaging in RWE analytics. Those categories of barriers are described in.Table3

Table 3 Factors that influence access to and use of RWE. Standards defining the content and quality of RWE are yet to be adopted

- Common terminology standards are still lacking
- Existing data remains incomplete
- Data quality assurance system remain underdeveloped

These limitations include (Int10; Avillach et al., 2013.[25]

- consistency of data entry
- coding errors
- discontinuities in data collection (missing data points)
- Inaccuracy (eg misdiagnosis).

Methodological barriers are limiting efficient use of RWE available

- Analytic capabilities are limited
- Dataset linkage poses methodological challenges Governance structures are influencing access to data
- There is a lack of clear pathway to access
- Data access is often only granted to academic researchers
- Lack of awareness among professionals can be detrimental

Privacy concerns are limiting the amount of data available and the scope of their use

- Ethical concerns amongst health professionals
- Medical data protection: a major concern for the public and European regulators
- Consent management constrains access to data

Barriers to enablers for access and use of RWE

The following table provides a brief overview of the study's findings. It summarizes the main barriers to access to and use of RWE and presents the types of strategies that are implemented to improve RWE access and use.

Table 4: Improving access to and use of RWE: from barriers to enablers

Barriers	Strategies to improve access and use
Content and quality issues	
Terminology issues	Standardisation of codes
incomplete data	Longitudinal data collection
Data quality issues	Processes for data quality assurance
Methodological barriers	
Limited analytics capabilities	National eHealth strategies
Lack of Analytical standards	Transnational and multisectoral coalition of experts
Linkage Challenges	European projects and best practices
Fragmentation	Interoperable systems
Governance structures	

Lack of clear pathway	Buying the data
access granted to academics only	Hiring/ partnering with academics
Lack of data controller engagement	Incentives for clinicians
Privacy Practices	
Ethical concerns among professionals	Trusted third party, depersonalisation tools
Ethical Concerns among the public	Communication Campaigns
Consent management	Liberal national strategies and innovative consent management tools

Indian Healthcare Scenario and RWE

Healthcare scenario today in India is a curious mix bag of immense opportunity and complex challenges where innovations/interventions and affordability are sides of same coin. This is essentially a very imperative requirement to the financial security for a country like India.

There are unprecedented healthcare challenges in India today that demand immediate attention and action. The most critical aspect among these is ensuring safety, efficacy, quality, affordability and accessibility of medicines and treatment to patients at all times. The key imperatives to overcome these continual challenges and catalyze the transformation include putting patients first, fostering innovation, and enhancing access.

While infrastructure improvement, capacity addition and development of manpower are critical for the Indian healthcare sector, it is also necessary that the existing facilities are operated in an efficient manner. This can be ensured through various means such as Accreditation, adoption of Cost Accounting Procedures and finally increased penetration of Healthcare Insurance.

Innovative technologies, processes and partnerships forged by the Indian government and private companies have begun bridging the health care gap. A multi-pronged approach from key stake holders is necessary to address the issue. Both the public and private sector need to work in tandem to make healthcare available, accessible and affordable. India would need various solutions towards this end.

Enhanced understanding and knowledge of health economics and its approaches and techniques, health systems research and health policy analysis is pivotal for efficient and effective utilization of resources. Compared to International standards of many other countries, Indian Public healthcare expenditure is very low. Policymakers today to direct investments in healthcare and to obtain the maximum benefit for the population as a whole utilize methodologies such as HTA and Health Economics and Outcome Research (HEOR). Payers of all types are set on demanding value for from expenditure on healthcare despite the predominance of out-of-pocket payments scenario.

Good understanding of analytical methods is central to more effective policy making for better health services, strategic capacity and skills to do so, has been one of the key challenges.

RWE is becoming an increasingly important element of healthcare decision-making as HTA and reimbursement agencies and payers become more demanding in terms of the relevance of clinical evidence and connections to the delivery of care in clinical practice.

Real-world evidence can provide inputs into many elements of the market access strategy, from choice of comparators in pivotal trials to development of economic models.

- Treatment pattern surveys among clinicians provide critical insight and understanding of current drug use, patient selection, treatment decision drivers, and relevant comparators in individual markets.
- Burden of illness studies provide critical insight into the impact of a disease and its treatment on patients and care givers, and provide a platform to understand the economic impact of potential changes in treatment.
- Resource utilization studies provide inputs into budget impact estimates and cost-effectiveness analyses that reflect real-world clinical practice.

Challenges in India are similar to those seen in the developed countries. Lack of electronic data gathering and the reliability of the same remains the major concern. There is also a lack of knowledge regarding the utility of the RWE between all stakeholders. Who should be investing in RWE is also a major contentious issue. Education and training of personnel on RWE remains a critical issue. Considering the current regulatory challenges for clinical trials in India, RWE can be helpful in answering various important issues related to effectiveness, safety and economic outcomes in Indian setting with real time data.

Healthcare organizations also need a technology infrastructure for managing and interrogating these complex information sets.

Characteristic challenges faced Indian Health care environment today includes inadequate infrastructure , constrained health care delivery work process which further increase the complexity.

Other challenges for the Indian health care system for IT integrating include:

- Lack of standards
- Lack of in-house IT domain knowledge
- Reluctance of medical, nursing and other staff to adjust to change
- Apprehensions around technology failures (paper systems appear more reliable)
- Lack of proper vendor support
- Cost/Benefit Analysis

It is estimated that 15% of India's population currently has no access to proper health care services, either due to due to availability and economic reasons. Statistics of practicing doctors reflect that 75% of the them practice in urban areas and 23% in towns, while only 2% practice in rural areas. One should aim to bridge this huge gap in healthcare delivery by increasing use of technology to help it reach a larger set of people.

SUMMARY

By investigating current forms and uses of RWE, there is a significant potential for assessing the (short- or long-term) impact of different drugs/devices or medical treatments and for informing and improving healthcare service delivery. Even though the potential use of RWE use seems quite clear, there are barriers that limit further development towards the full exploitation of this type of data. Factors limiting the potential benefits driven from RWE analysis have been identified. These include the absence of common standards for defining the content and quality of RWE (absence of common terminology, incomplete datasets, and lack of data quality assurance systems) and several methodological barriers (absence of standards for RWE analysis and for data linkage). Access to this type of data is also restricted by the lack of governance standards including the absence of standards for collaboration between stakeholders active in the field of RWE, and by the limitations of incentives for data sharing. Finally, privacy concerns (e.g. ethical concern among health practitioners) and privacy practices (e.g. personal data protection regulation) influence the amount of data available and the scope of its use. These issues are being addressed in uneven and at different levels by unstructured initiatives by both public and private stakeholders. For example, primary point in RWE that is data quality is controlled through European and international initiatives aiming to improve the standardization of terminology (e.g. ORPHANET in the field of rare disease). To facilitate best practice sharing and knowledge, development of international research coalitions is now highly encouraged. These practices also progressively help to develop common framework that may guide RWE collection and use. These initiatives thus contribute help improve both data quality and analytical capabilities of researches. A strong push towards the development of EHRs – and eHealth infrastructures more has been seen in some broadly – has been observed in some European countries and supported by the EU over the last six years through various schemes (e.g. FP7 Health Programme). These steps offer infrastructure of great potential for the automated and routine collection of patient data. Last parameter, access – which is related to both governance and data protection issues and problematic mostly for private companies – can be granted through the implementation of strategic partnerships among stakeholders (e.g. for specific research projects engaging directly with academics, with physicians in exchange of technological and analytical services and also with data vendors). Development of online consent management architecture will help aid to structure RWE in future.

REFERENCES

1. Holtorf AP, Watkins JB, Mullins CD and Brixner D, Incorporating observational data into the formulary decision-making process—summary of a roundtable discussio, J Manag Care Pharm, 2008; 14(3): 302–08.
2. West DM, Improving Health Care through Mobile Medical Devices and Sensor, Centre for Technology and Innovation at Brookings, 2012.
3. Eichler HG, Abadie E, Breckenridge A, Leufkens H and Rasi G, Open Clinical Trial Data for All? A View from Regulator, PLoS Med., 2012; 9(4).
4. Eichler HG, Pétavy F, Pignatti F and Rasi G, Access to patient-level trial data – a boon to drug developer, New England Journal of Medicine, 2012; 369(17): 1577–1579.
5. ISPOR Real World Data task force: Using real world data for coverage and payment decisions: The ISPOR real world data task force report.
6. Herland K, Akselsen JP, Skjonsberg OH, How representative are clinical study patients with asthma or COPD for a larger 'real life' population of patients with obstructive lung disease? , Respir Med., 2005; 99: 11–19.
7. Helfand M, Berg A, Flum D, et al. for the Patient-Centered Outcomes Research Institute Methodology Committee. Draft methodology report: 'Our questions, our decisions: standards for patient-centered outcomes research'. 2012. MethodologyReport-Comment.pdf (accessed 1 Feb 2013).
8. Berger ML, Dreyer N, Anderson F, et al. Prospective observational studies to assess comparative effectiveness: the ISPOR good research practices task force report, Value Health, 2012; 15: 217–30.
9. Chalkidou K, Tunis S, Whicher D, et al. The role for pragmatic randomized controlled trials (pRCTs) in comparative effectiveness research. Clin Trials, 2012; 9: 436–46.
10. Jonathan Stuart Ward, Adam Barker Undefined By Data: A Survey of Big Data Definitions - http://arxiv.org/abs/1309.5821
11. IBM BAO Strategic IP insight platform (SIIP), http://www-935.ibm.com/services/us/gbs/bao/siip/. Last accessed 19/01/2014.

12. Stroetmann KA, Artmann J and Stroetmann VN, European countries on their journey towards national eHealth infrastructures: Final European Progress Report, Brussels: DG INFSO and eHealth Strategies, 2011.
13. Franchi1 CG, Giussani P, Messina M, Montesano S, Romi A, Nobili I, Fortino A, Bortolotti L, Merlino and E. Beghi, Validation of healthcare administrative data for the diagnosis of epileps, Journal of Epidemiology and Community Health, 2013; 67(12): 019–1024.
14. IBM Institute for Business Value, Analytics: The real-world use of big data in healthcare and life sciences. How innovative healthcare and life sciences organisations extract value from uncertain data, Somers (NY): IBM Global Services, 2013.
15. Price D, Asukai Y, Ananthapavan J, Malcolm B, Radwan A and Keyzor I, A UK-based costutility analysis of indacaterol, a once-daily maintenance bronchodilator for patients with COPD using real world evidence on resource us, Applied Health Economics and Health Policy, 2013; 11(3): 259–274.
16. Gonzalez-Ruiz A, Beiras-Fernandez A, Lehmkuhl H, Seaton RA, Loeffler J and Chaves RL, Clinical experience with daptomycin in Europe: the first 2.5 year, Journal of Antimicrobial Chemotherapy, 2011; 66(4): 912–919.
17. Moat NE, Ludman P, MA de Belder, Bridgewater B, Cunningham AD, Young CP and Mullen MJ, Long-term outcomes after Transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis, Journal of the American College of Cardiology,2011; 58(20); 2130–2138
18. Banerjee AD, Lane C, Torp-Pedersen and G.Y Lip. Net clinical benefit of new oral anticoagulants (dabigatran, rivaroxaban, apixaban) versus no treatment in a 'real world' atrial fibrillation population: A modelling analysis based on a nationwide cohort study." Thrombosis and Haemostasis, 2012; 107(3): 584–589.
19. Coloma PM, et al., "Electronic healthcare databases for active drug safety surveillance: is there enough leverage?", Pharmacoepidemiology and Drug Safety, 2012; 21(6): 611–621.
20. Health Search Database (HSD); General Practice Research Database (GPRD); Norwegian Patient Register, Danish Civil Registration System (DCRS); Integrated Primary Care Information Project (IPCI); National Health Registers in Sweden; the Finnish Care Register for Health Care (HILMO); BIFAP; Sicily Regional Database (Italy).
21. VAESCO, "About Us," http://vaesco.net/vaesco/about-us.html, accessed 04/12/2013 Population figures for Finland, Spain and Sicily are not obtainable from the project documentation. While some of the results and data from the project are available through the website, data from the individual countries continues to be subject to authorisation by the relevant national organisations.
22. Lothgren M, et al. Cost per patient and potential budget implications of denosumab compared with zoledronic acid in adults with bone metastases from solid tumours who are at risk of skeletal-related events: an analysis for Austria, Sweden and Switzerland European Journal of Hospital Pharmacy: Science and Practice, 2013.
23. Roggeri DP, Roggeri A, Rossi E, Cinconze E, De Rosa M and Maggioni AP, Direct healthcare costs and resource consumption after acute coronary syndrome: a real-life analysis of an Italian subpopulation, European Journal of Preventive Cardiology, 2013:1–7.
24. Association of the British Pharmaceutical Industry (ABPI), Big Data Road Map, London: 2013.
25. Avillach, P, et al., Harmonisation process for the identification of medical events in eight European healthcare databases: the experience from the EU-ADR project, Journal of the American Medical Informatics Association, 2013; 20: 184–192.