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Integrating Real-World Evidence (RWE) in Oncology Drug Regulation: A Comparative Analysis of CDSCO and Health Canada

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ABSTRACT

Cancer remains a major global health challenge, necessitating continuous innovation in oncology therapeutics. While randomized controlled trials (RCTs) are the traditional gold standard for evidence generation, they often lack applicability to diverse real-world populations. This has fuelled growing interest in incorporating Real-World Evidence (RWE), derived from Real-World Data (RWD), into regulatory decision-making processes, especially in oncology. This study aims to compare how RWE is integrated into oncology drug regulation by two key regulatory bodies, Health Canada and India's Central Drugs Standard Control Organization (CDSCO), in order to identify lessons and opportunities that can support India's evolving regulatory framework. A qualitative comparative analysis was conducted using regulatory documents, guidance frameworks, and real-world case examples. Canada's CanREValue initiative was explored in depth, alongside an assessment of India's emerging digital health infrastructure and policy efforts. Health Canada has established a mature RWE framework supported by multi-stakeholder collaborations and pilot projects, facilitating dynamic regulatory decisions in oncology. In contrast, CDSCO is in the early stages of RWE adoption, with limited formal guidance. However, initiatives like the Ayushman Bharat Digital Mission (ABDM) and national health registries offer promising pathways. Canada's regulatory progress offers valuable insights for India. Strengthening digital infrastructure, developing national RWE frameworks, and fostering collaboration could transform India's oncology regulatory ecosystem. This study highlights the potential of RWE to improve evidence-driven decision-making and enhance access to cancer therapies.

Keywords: Real-World Evidence, Oncology, Drug Regulation, CDSCO, Health Canada, CanREValue

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INTRODUCTION

Real-World Evidence (RWE) is derived from Real-World Data (RWD), this phase involves the application of the Real-World Data to the Real-World Evidence and consists of the patient health data that is regularly gathered without randomized control trials (RCTs). Other sources that add to this pool of data include electronic health records, insurance claims, disease registries, and patient-reported outcomes. In contrast to some traditional clinical trials, RWE considers the dynamics of different patient groups and clinical practice at the population level and long-term outcomes of treatments in real-life scenarios.

As the scope of RCT undergoes and continues to expand limitation due to cost, time-consuming issues, and inability to explore and test restricted segments of the population, regulatory bodies and other healthcare

stakeholders are starting to use RWE as a supplementary source of evidence. Managing rare cancers There is much potential to use RWE to inform drug approvals, label expansion, and post-marketing surveillance in oncology, where decisions need to be made quickly and where there is generally little available trial evidence.

The world is developing towards regulation to adjust to this change. Whereas countries such as the United States FDA and European Medicines Agency (EMA) have implemented guidelines on the utilization of RWE, others such as Canada and India are still in different phases of formalizing its application. Canadian regulatory system has launched specialized programs such as CanREValue whereas India is at starting points of the digital health revolution but is actively interested in the use of RWD to support regulatory and clinical decision-making.

Overview of Health Canada

The federal department that is mandated with the health and safety protection and improvement of Canadian people is the Health Canada. It is the main regulatory body of drugs, biologics and medical devices as well as of other products that affect health, working in the frame of Food and Drugs Act and other important legislative platforms. The vision of Health Canada focuses on a strong, transparent, and evidence-based regulatory policy which aims to maintain a healthier product in the market, in terms of quality, efficaciousness, and security of the therapeutic products which enter its frontier.

The process of drug approval drug in Canada is a tiresome process that is encompassed of several stages. First, the drug developers can have pre-submission conferences where the expectations and requirements can be explained. After this, the developer will proceed to make the New Drug Submission (NDS) with full illustration of information relative to the safety, efficacy and quality

on the product. The submission is also subject to the intensive scientific assessment by the pertinent directive (TPD or BGTD) and this process may incorporate consultations to the expert advisory committee in cases where it seems necessary. Should the review exhibit a favorable outcome, Health Canada grants a Notice of Compliance (NOC), which allows entry in the market, and gives the drug a Drug Identification Number (DIN), a formal approval. This multiple layered regulatory model provides a balance between giving access to new therapies and safeguarding the health of the population by scientific rigor.

Real-World Evidence (RWE) is gaining importance in the oncology drug regulation. Although conventionally RWE is used as a supplement to post-market safety surveillance, Health Canada is starting to embrace the use of RWE in regulatory decision-making especially in post-market settings or label extension in a rare cancer population. One such application is in post-approval monitoring of safety in immune check point inhibitors like nivolumab (Opdivo) and pembrolizumab (Keytruda). These medicines were approved by NOC/c on various indications, and the effectiveness and safety of the related medicine were also reinforced by real-world databases of various types of patient populations in non-controlled conditions.

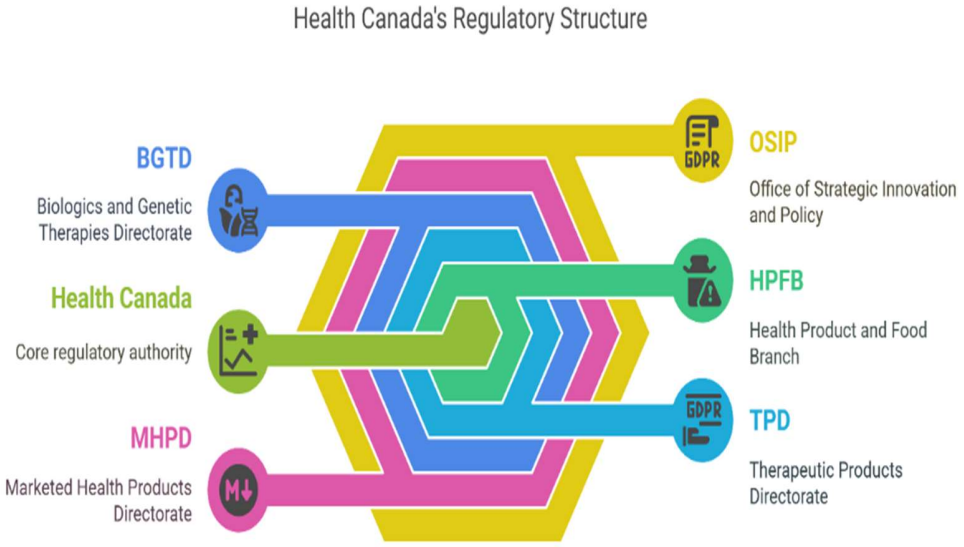

Figure 1: Health Canada's Regulatory Structure

Real-World Evidence (RWE) is gaining importance in the oncology drug regulation. Although conventionally RWE is used as a supplement to post-market safety surveillance, Health Canada is starting to embrace the use of RWE in regulatory decision-making especially in post-market settings or label extension in a rare cancer population. One such application is in post-approval monitoring of safety in immune check point inhibitors like nivolumab (Opdivo) and pembrolizumab (Keytruda). These medicines were approved by NOC/c on various indications, and

the effectiveness and safety of the related medicine were also reinforced by real-world databases of various types of patient populations in non-controlled conditions.

Furthermore, Health Canada, in its new regulatory strategy, is eager to work with its international partners including the U.S. FDA, European Medicines Agency (EMA) and International Council for Harmonization (ICH) to harmonize the standards and share the data especially oncology drugs that are being developed and introduced in different countries and regions. Such collaborations also increase the integration of RWE by establishing unified critiques and procedures of evidence assessment.

CanREValue initiative

Real-world Evidence for Value in Cancer (CanREValue) Initiative is a national coordinated activity to build a strong system of implementation of the Real-World Evidence (RWE) in Canadian drug lifecycle in the oncology space. This initiative, which began its work in 2017 and is headed by ICES (formerly the Institute for Clinical Evaluative Sciences) was a reaction to the growing interest in evidence on the clinical and economic performance of high-cost oncology medications in the real-world.

Very often, cancer treatments are registered with a small amount of evident trial results, sometimes even under a conditional framework like the Notice of Compliance with Conditions (NOC/c) which implies that substantially not much can be known about long-run effectiveness, safety and cost-efficiency. In this respect, CanREValue was conceptualized as developing an infrastructure to produce and integrate RWE at numerous thresholds in the life cycle of a drug, most especially its post-market phase.

The main goal of CanREValue is working out a pan-Canadian system enabling consistent creation and utilization of RWE in HTA (Health Technology Assessment), pricing and reimbursement policy and reappraisal of oncology drugs. This does not only consolidate improved clinical outcomes but also makes healthcare budgets sustainable, particularly, as the costs of emerging novel targeted and immuno-oncology agent surge. To accomplish this, five working groups are set where the roles of developing particular elements of the framework are distributed.

The essence of CanREValue is that RWE should be fit-for-purpose. In contrast to randomized controlled trials (RCTs), real-world data (RWD) sources like cancer registries, administrative claims, and EMRs do not contain enough quality and complete data. Thus, CanREValue highlights legible rules about the design of studies, protocol disclosure, and peer-review review of RWE reports. The potential of this method has been proven during pilot projects, e.g., the exploration of the survival rates and the treatment patterns of immunotherapy agents in the various provinces.

During the last few years, Canada has improved remarkably when it comes to codifying the use of Real-World Evidence (RWE) utilized in drug assessment. With the mounting pressure to bring novel therapies to market at an enhanced pace and, particularly, in oncology, the necessity of well-organized, transparent, and scientifically sound systems of RWE has significantly increased. Being aware of this, Health Canada, as well as CADTH (Canadian Agency for Drugs and Technologies in Health), developed guidance documents and participated in pilot projects that examine how RWE can effectively be used in the regulatory and health technology assessment (HTA) context.

In 2019, Health Canada began a consultation on RWE by issuing its discussion paper entitled: Real-World

Evidence: Informing Regulatory Decision Making, which set out the various circumstances where RWE might assist in a regulatory decision to approve drugs, including new uses and safety monitoring (after the drug is on the market). The document also highlighted that despite the fact that RCTs are the gold standard as regards to the establishment of efficacy, RWE could help add to the information regarding these fields, by being able to determine if the long-term developments of the results are commendable, how rare type of adverse events occur and also how effective the given is on wider and a more diverse population. The approach adopted by the health Canada parallels international developments and is comparable to the initiatives of the FDA in the RWE Framework and the Adaptive pathways developed by the European Medicines Agency.

Subsequently, Health Canada launched regulatory pilot projects with industry stakeholders trying using real-world data in new indications and changes to labels. These pilots tested real-world end points, approaches to data curation and the acceptability of study designs -- including retrospective cohort analyses of provincial administrative health data. Such pilots created a framework that will continue to be used in further RWE opportunities application with regulatory submission, creating capacity internally in the agency and expectations in the industry.

Concurrently, CADTH has released a reassessment RWE guidance, especially in its post-market drug evaluation program. During 2021 CADTH published a framework of the Use of Real-World Evidence to Support Post-Market Drug Reassessment, whereby payers can reconsider funding decisions. This applied especially to oncology where, the first funding is usually made on uncertain grounds and has to be reviewed after some time. The areas of importance that CADTH RWE framework stress is the sources of data required, analysis strategy, governance, and cost-effectiveness and clinical impact decision-level thresholds.

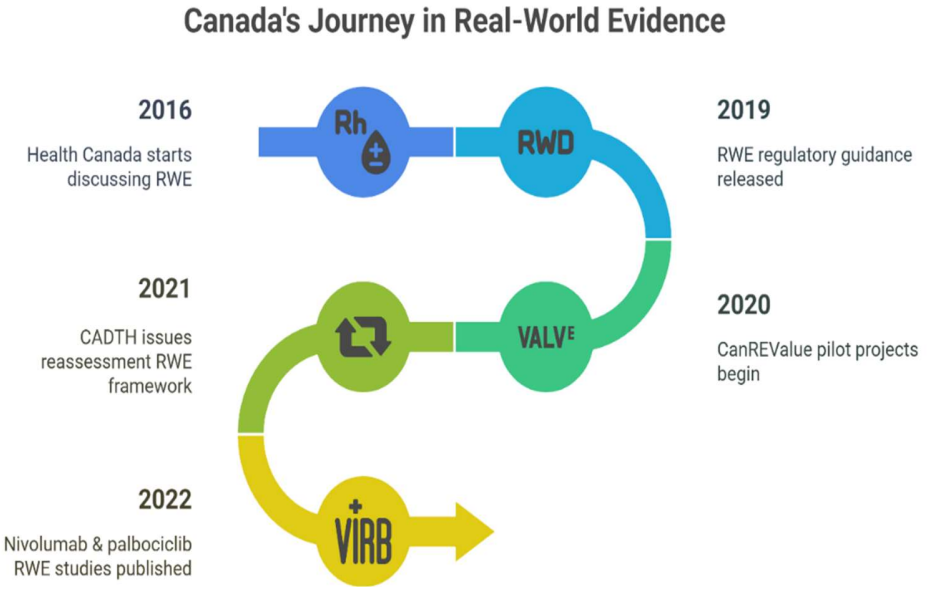

Figure 2: Canada's Journey in RWE

On top of these regulatory and HTA activities, the CanREValue Collaboration has had several RWE pilot studies with the support of provincial cancer agencies. This group of pilots tested the outcomes of the active therapy and use of many immuno-oncology agents in the non-small cell lung cancer (NSCLC). The researchers could use population-based cancer registries, pharmacy claims, and mortality databases to evaluate such outcomes as overall survival, time of disrupting treatment, and the utilization of healthcare resources beyond trials.

A well-known CanREValue pilot has employed real-life data of Ontario and British Columbia to study post-market performance of nivolumab within patients with advanced NSCLC. This paper gave us some idea of the way the drug worked in older people and in individuals with multiple medical conditions- two groups not usually inculcated into clinical trials. Findings were in agreement with the RCT study and further supports the evidence base to reimburse ongoing benefits in the public plans. Also, the study showed that it is possible to perform pan-Canadian RWE studies with harmonized research strategies and connections between data resources, which opens a gateway to national-level evaluations.

The other example is that of the reassessment of palbociclib in metastatic breast cancer. First sanctioned via a conditional NOC/c pathway, earlier clinical experience led to follow-up HTA and funding modifications in a number of provinces as a result of real-world data. The experiences of these types of RWE were used to explain the selection and modification of treatment criteria, dosage adjustments, and monitoring. This contributes to increasing the clinical value and cost-effectiveness.

Overview of CDSCO(India)

The Central Drugs Standard Control Organization (CDSCO) is the top agency in India that administers health care products and medical equipment. CDSCO operates under the Ministry of Health and Family Welfare and is the National Regulatory Authority (NRA) responsible in the safety, efficacy, and quality of medical products in the Indian markets. It collaborates with State Drug Control Departments that allows making a dual regulation type where there is balance between central drug approvals, and decentral implementation and enforcement.

Under Drugs Controller General of India (DCGI), CDSCO deals with:

- New drug approval and clinical trials.
- Control of import and export of drugs and cosmetics.
- Regulation of biologics, vaccines and medical products.
- BA/BE data evaluation.
- Implementation of pharmacovigilance schemes on post market safety surveillance.

CDSCO is functioning under legal framework of:

- Drugs and cosmetics act, 1940
- Drugs and Cosmetics Rules 1945
- And just recently the New Drugs and Clinical Trials Rules, 2019 (NDCTR)

These regulations give an elaborate procedure on how the approval of new drugs, clinical trials and investigational new drugs (INDs) are to be facilitated adding clarity to the specifications of ethics committee duties, responsibility of sponsor and commitments after marketing.

The regulatory provisions are also issued as regulatory guidance documents and standard operating procedures (SOPs) by CDSCO in order to facilitate quicker and more transparent interactions on the regulatory front. It regularly works with other regulatory bodies across different countries including the US FDA, EMA, and WHO in mutual harmonization initiatives within ICH (International Council for Harmonization) and PIC/S.

The CDSCO operates on two levels, the central office in New Delhi, with support staff in:

- 6 Zone Offices (Mumbai, Kolkata, Chennai, Ghaziabad, Hyderabad, Ahmedabad)
- 4 Sub-Zonal offices
- 13 Port Offices
- 7 Central drug testing laboratories

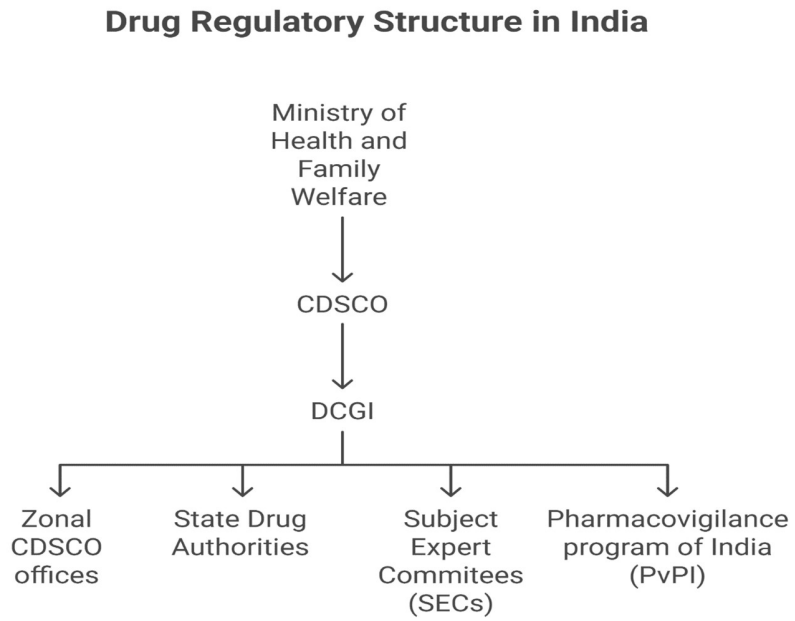

Figure 3: India's Drug Regulatory Structure

Oncology is one such area of therapy in which quick access to new therapies matters a great deal. The increased burden of cancer in India, approximated at a rate of more than 1.5 million new cases per year (ICMR, 2021), has already resulted in the need to embrace more accommodating regulatory framework to satisfy its treatment needs.

Although the agency is still concerned in making drugs in oncology and rare diseases available when and where they are needed, it also has a sound pharmacovigilance system in the form of Pharmacovigilance Program of India (PvPI) facilitated by the Indian Pharmacopoeia Commission (IPC). But the recent activity of post-marketing surveillance is rather done on the grounds of safety (e.g., Serious Adverse Event [SAE] reporting, periodical updates of safety information) than on realistic effectiveness.

RWE Regulatory Decision-Making in India

Use of RWE in regulatory decisions in India is young. The regulatory authorities, US FDA, Health Canada and European Medicines Agency (EMA) have worldwide implemented regulatory pathways to include RWE in other aspects of drug life cycle, including pre-approval analysis and prioritized access, post-market review and policy update. Conversely, the Indian regulatory environment, led by the Central Drugs Standard Control Organization (CDSCO) is yet to incorporate RWE as an organized aspect of its decision-making and regulatory functions.

Although India is not yet equipped with a specific RWE policy or framework, some specific activity performed by regulating is indirectly associated with aspects of real-world data. These

mainly incorporate post-marketing surveillance (PMS), pharmacovigilance, and a family obligation Phase-IV studies mainly on drugs either receiving a waiver of a local clinical trial, or those approved under an accelerated course. To be specific, within the sphere of oncology CDSCO sometimes allows the marketing of drugs already approved in other jurisdictions with open regulatory practices, such as the United States of America or the European Union, without local testing in India. The regulatory body in such instances normally puts obligation on sponsor to carry out post marketing studies to track safety of the Indian population. These analyses are however more likely to study negative side effects of the drugs as well as safety hazards but would not take into account the overall effectiveness or comparison with other outcomes which RWE endeavors to document.

Despite the fact that real-world data are being generated in India based on hospital-based registries, electronic health records (EHRs), and observational studies, yet the information is not being utilized by CDSCO in a regulatory capacity in a regular manner. As an illustration, all the major cancer hospitals in the country, All India Institute of Medical Sciences (AIIMS), Tata Memorial Hospital, and privately owned networks, Apollo and Manipal administer retrospective and prospective observational research. Such studies can usually offer useful knowledge on the performance of drugs, patient compliance, and treatment

outcomes in a real-life scenario. The regulatory value of these data, however, is limited because it has no process in CDSCO to formally review this evidence or use it in making decisions when approving drugs, updating labels or bargaining drug prices.

However, change dynamic gives us relevance of future integration. The introduction to the National Digital Health Mission (NDHM) in Ayushman Bharat Digital Mission will produce a common digital health system nationwide. This entails both patient-specific health IDs as well as the patient EMR systems and data-sharing systems, all of which have the potential of establishing a large-scale RWE generation. There is further a National Cancer Registry Program (NCRP) sponsored by the Indian Council of Medical Research (ICMR) providing disease-specific information which, when extended and joined to therapeutic results, these may become a significant information source to oncology-related RWE.

Along with that, there is an increasing sense of appreciation about the usefulness of RWE in supplementing clinical trial evidence in an internationally diverse and high-population country such as India. There are many patient subgroups included in the trials condition that are still excluded in real-world data, including seniors, those who have comorbidities, or patients in a rural

location. Moreover, in situations when health budgets are restricted, RWE may provide important indicators of cost-effectiveness and trend use to improve more conscious healthcare choices.

Problems of adopting Real-World Evidence (RWE) in India

Although the interest in the same regarding real-world evidence (RWE) application in India healthcare system is growing, the prospect of the widespread use of RWE in the regulation decision-making is still a distant one. Though other countries like Canada or United States have achieved major success in integrating RWE into the approval process of drugs and into the country policy making process, India has some structural, technological, and regulatory prerequisites that impede progress in the same regard.

Data quality and standardization is a related issue. The records of patients in India are handwritten and incomplete or not properly maintained especially in the larger quarters of India. Inconsistency in clinical documentation procedures in different organizations implies that even when electronic records are provided, they may not include all important variables, including such variables as diagnosis codes, treatment workups, or follow-up results. Moreover, there is no consistent coding system such as ICD-10 or SNOMED CT among all providers in the healthcare sector which also makes it difficult to combine and analyze data on the national level. The non-standard model of formats does not only impede the interoperability, but causes suspicions about validity and reproduction of any results which were obtained using such data.

The other significant challenge lies in the fact that there is no official advice on RWE by the Central Drugs Standard Control Organization (CDSCO). In such jurisdictions as the U.S. and Canada, regulatory bodies have provided specific RWE frameworks, as well as the acceptable use cases, methodologies, and data sources. Conversely, CDSCO has not released any policy or guideline depicting how RWE can be integrated into drug submission, approval, or re-evaluation. Consequently, the pharmaceutical companies and research institutes have uncertainty over the issue of whether and how to design RWE studies to be used in the regulation within India. A lack of articulate expectations would mean that there is no great incentive of investing in large scale RWE programs to suit Indian regulatory submissions.

Another obstacle is the low supply of qualified specialists and practicable expertise in analytics. Interpretation and generation of RWE involves sophisticated concepts on epidemiology, biostatistics, informatics and health economics. India is a good source of both “pharma and IT talent, and used alongside regulatory-grade RWE, they are an emerging combination. In addition, the majority of administrative staff at CDSCO and state organizations are yet to receive proper

training in assessing the use of observational studies designs, detection of causal inference, or real-life study plans. This skill deficiency is found in the generation and regulation appraisal of RWE.

The use of real world data is also complicated by ethical and legal ramifications of patient privacy and data protection. Despite the fact that India enacted the Digital Personal Data Protection Act in 2023, its practical application is ambiguous throughout the healthcare system. The issues of consent, data sharing, and de-identification are a source of concern that makes hospitals, institutions, and researchers wary of dropping into centralized places of data. These doubts have the potential of impeding the creation of national registries and real worlds databases that are necessary to support massive RWE research studies.

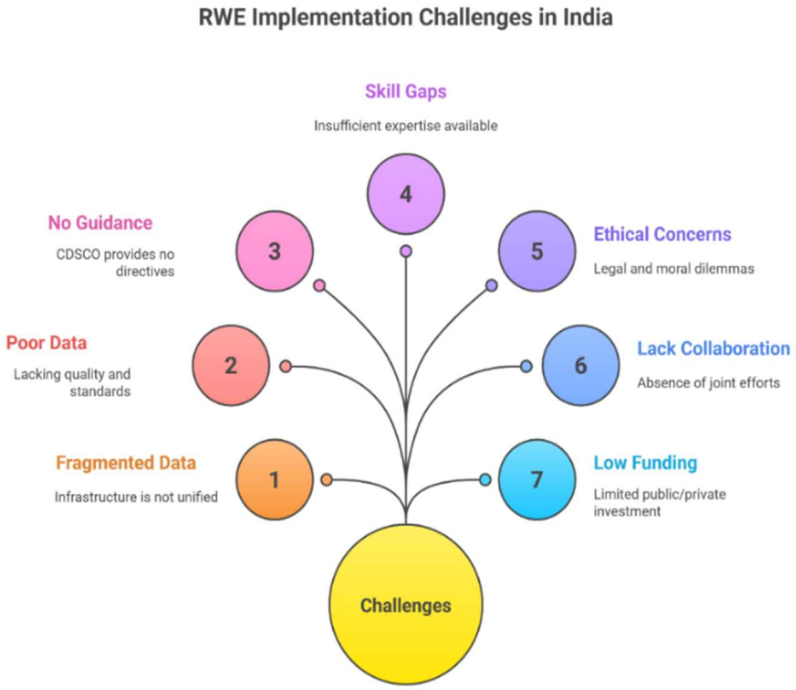

Figure 4: RWE Implementation Challenges in India

COMPARATIVE TABULATED ANALYSIS OF HEALTH CANADA AND CDSCO

Feature	Health Canada	CDSCO (India)
Formal RWE Policy	Structured guidance through CanREValue and associated Health Technology Assessment (HTA) bodies	No formal guidance yet, scattered use in post-marketing surveillance
Use in Pre-market Approval	Exploratory use via pilot projects	Not accepted, RCT remains the gold standard
Use in Post-market Surveillance	Strong integration; RWE supports conditional approvals and safety updates	Limited to Periodic Safety Update Reports (PSURs), minimal influence on regulatory decisions
Stakeholder Involvement	Inclusive, involving regulators, payers, clinicians, patients, and	Primarily regulator-driven with less multistakeholder input

	industry	
Key Initiative	CanREValue Initiative (2017–ongoing)	None yet specific to RWE
Digital Health Integration	Advanced EHR systems and national data repositories	Fragmented health records, limited EHR penetration
Transparency	High, publishes decision summaries and HTA reports using RWE	Low, few publicly accessible RWE reports or impact statements
Examples in Oncology	RWE used in CADTH submissions for rare cancers (e.g., CAR-T therapy reviews)	Limited case studies; RWE not directly cited in approvals
Infrastructure Readiness	High, presence of population-level databases and privacy laws like PIPEDA	In development, National Digital Health Blueprint (NDHB) and Ayushman Bharat Digital Mission (ABDM) are positive signs
Barriers	Harmonizing RWE methodologies across provinces; data privacy alignment	Data standardization, regulatory uncertainty, lack of trained workforce
Vision	To make RWE a co-equal with RCTs in decision-making	To develop a roadmap for RWE over the next decade (currently underexplored)

CONCLUSION

In this article, we have delved into the dynamic nature of real-world evidence (RWE) in drug regulation in the oncology sector where the analysis took a comparative approach in comparing the regulatory policies of the Health Canada and CDSCO. With the help of this analysis, it has become clear that although both countries are moving towards capitalizing on the usefulness of the RWE, Canada has developed a more organized systemic concept, in particular, with such a program as CanREValue. Conversely, the regulatory system of India is at an early phase of formal RWE integration. The comparative analysis shows that CDSCO has a great scope to adopt and adapt global best practices not only to speed up oncology approvals, but also as a way of making decisions more inclusive, timely and decision-based. Both India and the global healthcare sector have the opportunity to harness large volumes of demographic data and an enormous pool of patients with the help of regulatory framework, policy, and inter sector coordination. The findings highlight that CDSCO can benefit from global best practices to enhance regulatory efficiency and accelerate access to cancer therapies. In the rapidly evolving landscape of oncology, RWE can no longer remain a supplement, it must be central to regulatory innovation. Embracing RWE is not the question of choice as the future of drug regulation does not exist within the limits of the randomized clinical trial. However, it is particularly vital in the field of oncology where providing timely access to effective drugs can be a difference between life and death. It is the hope of this project that it will act as a stepping stone to further research, discussions and changes that can

close the regulatory gaps and eventually result in a positive change in the outcomes of cancers everywhere across the world.

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