MINISTRY OF HEALTH MALAYSIA

A QUICK GUIDE TO USING REAL-WORLD EVIDENCE (RWE) IN MALAYSIAN HTA

INFORMING POLICY, STRENGTHENING DECISIONS

GUIDANCE FOR INTEGRATING RWE INTO HEALTH TECHNOLOGY ASSESSMENT PRACTICE

MAHTAS

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CHAPTER 1

INTRODUCTION

This document provides a quick guide to using Real-world Evidence (RWE) for health technology assessment (HTA) in Malaysia. The guidelines incorporate input from stakeholders at the **Policy Development Workshop on Real-World Evidence (RWE) for Health Technology Assessment in Malaysia**, held from March 19 to 21, 2023. The primary references for this guidance are these five published guidelines for best practices of RWD and RWE; namely:

1. Guidelines on Patient Registry Establishment and Implementation in Ministry of Health Malaysia[1]
2. REALISE - Use of Real-World Data and Real-World Evidence to Support Drug Reimbursement Decision-making in Asia[2]
3. NICE Real-World Evidence Framework[3]
4. Real-World Evidence Framework to Support EU Regulatory Decision-Making[4]
5. Optimising The Availability and Use of Real-World Data and Real-World Evidence to Support Health Technology Assessment in Australia[5]

Purpose:

- This guidance establishes a comprehensive framework for generating and utilising RWE for HTA in Malaysia.
- Its primary goal is to standardise the processes of data collection, analysis and application.
- This ensures that RWE used in HTA is robust, relevant and reliable for decision-making.

RWE's Role:

- RWE is crucial for evidence-based medicine and HTA, offering valuable insights into health technology performance, cost-effectiveness and real-world impacts.
- It serves to supplement traditional clinical trial data, effectively filling evidence gaps, particularly for rare diseases or emergency conditions where randomised controlled trials (RCTs) may be unfeasible.
- Furthermore, RWE plays a vital role in supporting post-market surveillance, monitoring the long-term safety and effectiveness of health technologies once they are in general use.

Current Use:

- In Malaysia, RWE is already actively utilised in HTA to inform various aspects of healthcare decision-making.
- Examples include its application for epidemiological data, safety assessments, and evaluations of organisational, social, ethical and economic impacts.

Potential Uses:

- RWE can strategically enhance HTA by providing critical information for diverse areas.
- This includes informing policy and coverage decisions, such as assessing and reassessing health technologies and supporting Managed Entry Agreements (MEA).[6]
- It also extends to monitoring and surveillance activities like performance monitoring and ongoing post-market surveillance, and crucially, incorporates patient-centred outcomes through Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs).[7, 8]

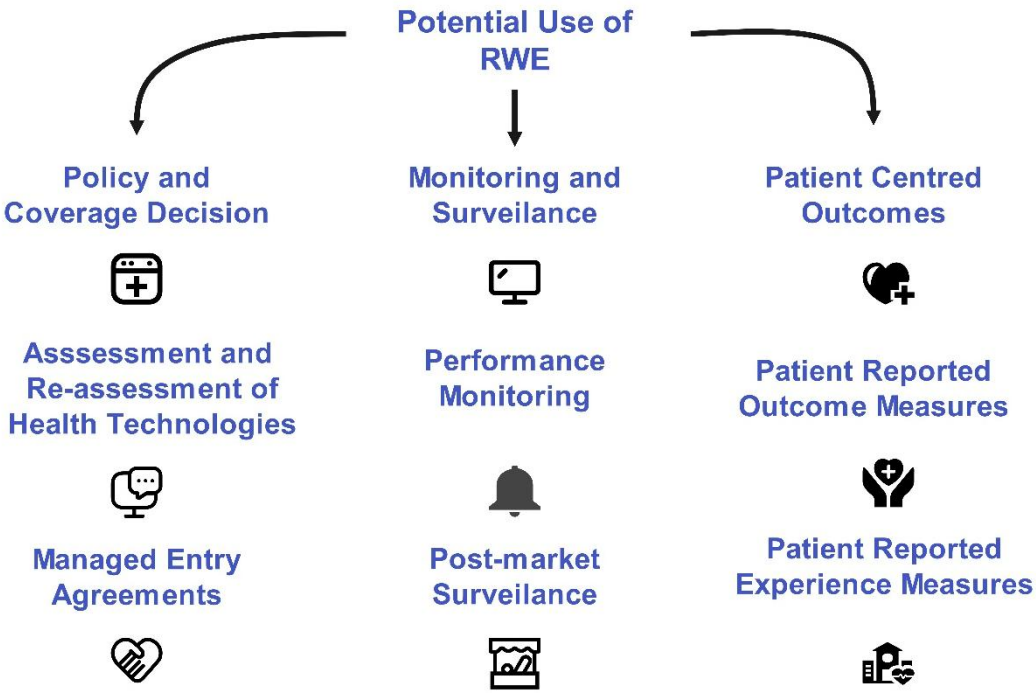

Figure 1.1 Potential Use of RWE

Quality of RWE:

- The quality of RWE is paramount for ensuring that HTA decisions are accurate and reliable.
- Achieving high-quality RWE necessitates standardised processes for data collection, evaluation and utilisation across all stages.
- This commitment to quality ensures the trustworthiness and applicability of the evidence in real-world healthcare contexts.

CHAPTER 2

DEFINITIONS, TYPES AND SOURCES OF REAL-WORLD DATA

Definitions:

- Real-world Data (RWD) refers to health-related data routinely collected during standard healthcare delivery, encompassing sources like electronic medical records, claims, registries and patient-generated information.[9]
- Real-world Evidence (RWE), on the other hand, is the clinical evidence and insights derived from the analysis of this RWD.[9]

Types of RWD:

- RWD in Malaysia is categorised into several types based on its nature and collection context, providing comprehensive insights for HTA.
- These include Clinical Data (patient demographics, outcomes), Economic Data (healthcare costs, resource utilisation), Utilisation and Surveillance Data (technology usage, side effects), Patient-Reported Outcome Measures (PROMs) & Patient-Reported Experience Measures (PREMs) (patient perspectives) and Epidemiological Data (disease prevalence, incidence).

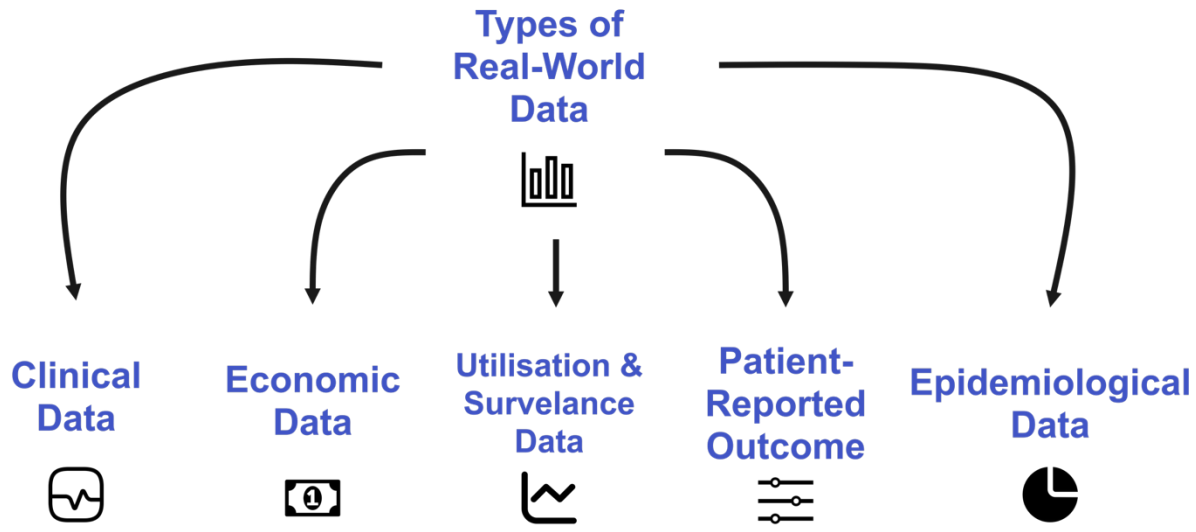

Figure 2.1 Types of Real-World Data

Sources in Malaysia:

- Malaysia boasts diverse sources of RWD crucial for generating relevant and reliable RWE.
- These include numerous National Registries (e.g., Acute Stroke, Cancer, Renal), Electronic Health Records (MyHDW, MPIS) and data from Claims and Billing Activities (Casemix Database, Peka B40).

- Additionally, Pharmaceutical Data (PhIS, MyPriMe), Economic and Financial Data (MNHA, IGFMAS), and various other sources, such as DOSM, IRBM and MySejahtera, contribute to the rich data landscape.

Metadata:

- Understanding metadata, which is "data about data," is crucial for effectively utilising RWD.
- It provides essential context, such as timestamps of entries, the healthcare professional who recorded the data and specific codes for diagnoses or procedures.
- This detailed information ensures clarity, reproducibility and proper interpretation of the raw clinical data.

Emerging Sources:

- The landscape of RWD is evolving, with mobile health technologies like wearable devices and mobile applications becoming increasingly important sources.[2, 10]
- These devices continuously generate data on physiological parameters and activity levels, which can be linked with contextual information like location.[5, 10]
- Furthermore, environmental factors and social media platforms are emerging as valuable sources, offering insights into health outcomes and population-level behaviours.[10]

Limitations:

- Despite the richness of RWD sources, several limitations must be acknowledged to ensure responsible use.
- Key challenges include concerns about data quality, privacy protection and the representativeness of the collected data.[3]
- Addressing these issues through careful validation and responsible data management is crucial for the effective and reliable use of data in regulatory and HTA decision-making.

CHAPTER 3

ESSENTIAL PARAMETERS OF REAL-WORLD DATA

Real-world Data Parameter:

- The careful identification and establishment of essential parameters within RWD is a critical step for conducting a comprehensive HTA.
- These parameters ensure that the collected data is relevant and sufficient to provide meaningful insights into health interventions.

Figure 3.1 Essential Parameters of Real-World Data

Sociodemographic & Socioeconomic Parameters:

- These parameters are vital for evaluating the equity and accessibility of healthcare interventions and understanding the population impacted by health technologies.
- Key elements include age, gender, occupation and education, which help discern variations in illness patterns and health literacy.
- Furthermore, individual/household income and the source of payment for healthcare are essential for assessing affordability and identifying financial barriers to accessing health technologies.

Resource Utilisation Parameters:

- Data on resource utilisation is essential for assessing the efficiency and cost-effectiveness of health technologies in real-world settings.
- This includes information on the types of facilities where technologies are used, detailed records of diagnoses, treatments and procedures, and the frequency of visits and length of hospital stays.
- Clinical parameters and Malaysian DRG (MyDRG) data also provide crucial insights into resource allocation and the strain on the healthcare system.

Patient Outcomes Parameters:

- Patient outcomes represent the definitive criteria for evaluating the efficacy of health technologies, reflecting the results of patient care and management.
- Key parameters include the primary diagnosis and associated complications, offering an extensive perspective on disease burden and the technology's impact.
- Additionally, quality of life (QOL) metrics, such as PROs and PREMs, provide a comprehensive view of patient well-being, while mortality data helps understand the effects of diseases and therapies.

CHAPTER 4

DATA GOVERNANCE

Definition:

- Data governance is a comprehensive strategy for the overall management of data, ensuring its usability, availability, integrity, quality and security.[11]
- Its purpose is to maximise the potential of data assets by providing oversight that guarantees consistency, accuracy, and appropriate use.
- This framework is crucial for maintaining trust and reliability in RWD and RWE.

Data Quality and Credibility:

- Data quality refers to the reliability and accuracy of data, which is crucial for the trustworthiness of RWE, especially for HTA.[5, 6]
- Credibility is influenced by factors such as data quality and consistency, potential biases and measurement errors, and the transparency of data provenance and relevance.
- Enhancing credibility requires methodological rigour, transparent reporting of data sources and governance, and continuous stakeholder engagement to build trust.

Data Standardisation:

- Data standardisation involves establishing and implementing uniform formats, definitions and terminologies for data elements.[1, 3, 6]
- This concerted effort is crucial for ensuring consistency, comparability and seamless interoperability of data across numerous sources and diverse systems over extended periods.
- Key tools include Common Data Models (CDMs) like OHDSI and adherence to national standards such as the National Health Data Dictionary and MyHRDM.[1, 3]

Data Privacy and Protection:

- Data privacy and protection are fundamental to the ethical and responsible use of RWD and the generation of RWE.
- Upholding legal and ethical obligations, such as compliance with Malaysia's Personal Data Protection Act (PDPA) and obtaining informed consent is compulsory.[12]
- Robust security measures, such as encryption, strict access control and de-identification techniques are essential to protect sensitive information and build public confidence.[1]

Data Accountability:

- A clear data governance structure and accountability are crucial for ensuring transparency and responsible management of RWD.
- In the Ministry of Health (MOH), the Registry Data and Information Governance Committee provides oversight and accountability.[1]
- Practices such as defining roles and responsibilities through clear statutes, conducting regular internal and external audits and providing transparency to stakeholders are imperative for maintaining high-quality RWD and compliance with governance standards.

CHAPTER 5

STUDY DESIGN AND ANALYSIS

Study Design:

- The rigour and appropriateness of the chosen study design are critical for generating credible RWE from RWD.
- Unlike controlled RCTs, RWD originates from routine healthcare practices, necessitating well-defined study designs to establish meaningful associations and infer causality.[10]
- A robust study design serves as the framework for systematically collecting and analysing RWD, playing a crucial role in mitigating inherent biases and confounding factors that can compromise the reliability of findings.[3]

Appropriate Study Designs for Generating RWE:

- Various study designs are suitable for generating RWE, each with specific strengths.
- These include Observational Studies (Cohort, Case-Control, Cross-sectional, Case Series) which observe subjects without intervention.
- Other designs include Pragmatic Clinical Trials (PrCTs), which evaluate interventions in real-world settings; Single-Arm External Control Trials, useful for rare diseases; Pre-post Trials for assessing changes over time; and Target Trial Emulation, which applies RCT principles to observational data to infer causality.[2, 3, 10, 13]

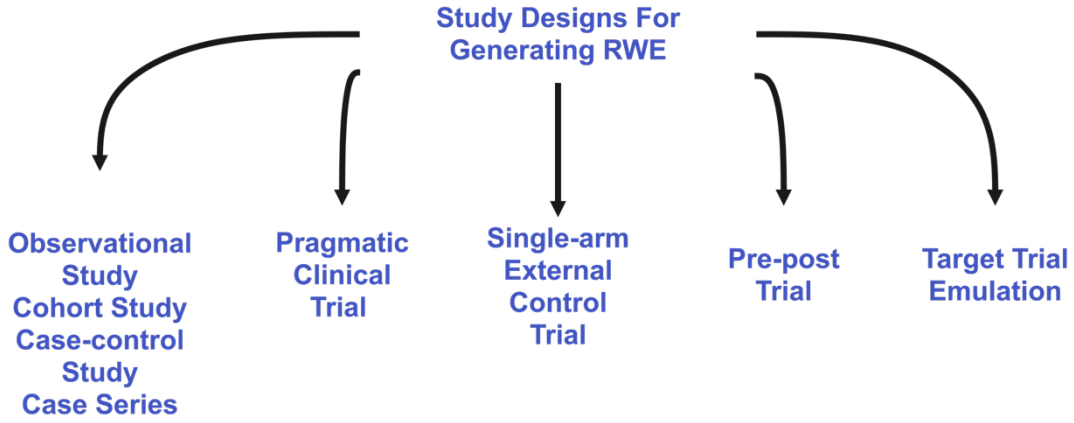

Figure 5.1 Study Designs for Generating Real-World Evidence

Methods to Analyse RWD:

- Analysing RWD to generate reliable RWE requires careful consideration of potential biases and confounding factors inherent in its observational nature.
- Conventional methods like restriction, stratification and matching are employed to address these issues during the planning and analysis stages of a study.

- Other methods include descriptive statistics to summarise data characteristics and inferential statistics to draw conclusions about populations.
- Crucially, various techniques are employed for addressing bias and confounding, such as Propensity Score Analysis (PSA), Covariate Adjustment, Instrumental Variable (IV) Analysis, Genetic Matching, G-Methods, High-dimensional Propensity Scores and Regression Discontinuity Designs.[2, 3]

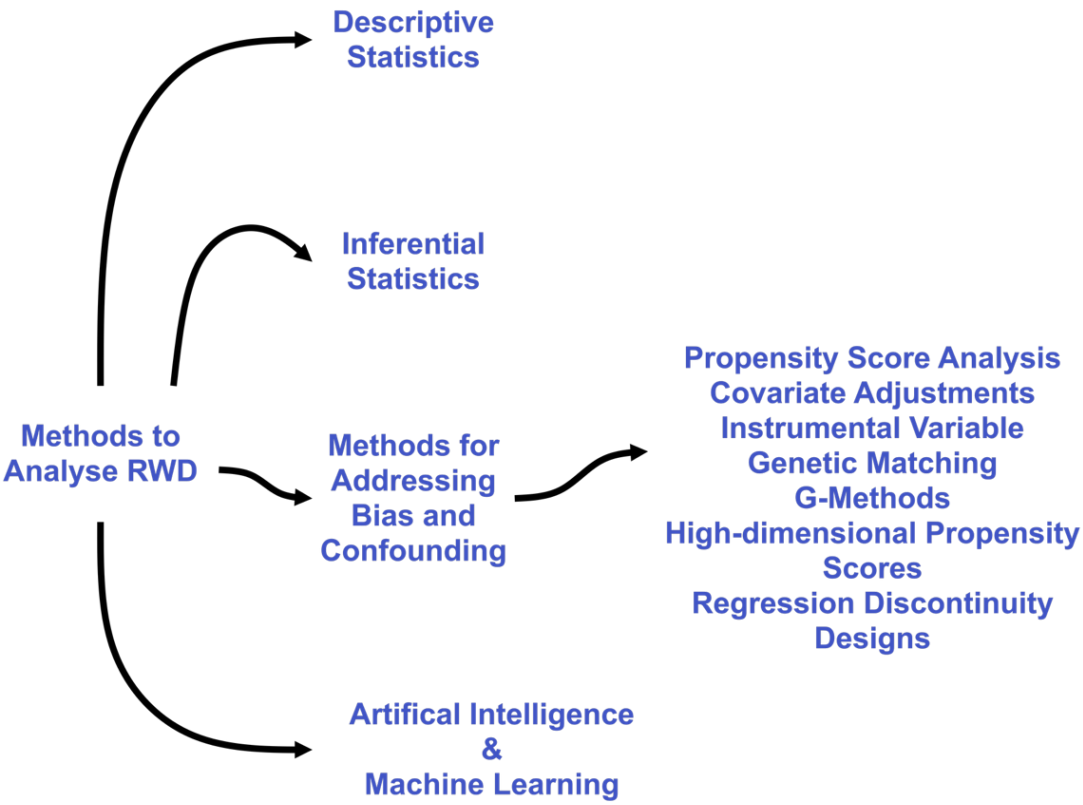

Figure 5.2 Methods to Analyse Real-world Data

Artificial Intelligence (AI) and Machine Learning (ML):

- AI and ML are increasingly recognised for their potential to transform RWD into valuable RWE, offering novel approaches to handle data complexities.
- Their applications include processing large, complex and unstructured data, identifying patterns, predictive modelling, fraud detection and improving data quality through cleaning and pre-processing techniques.[10]
- However, current applications are primarily focused on prediction and classification, requiring medical validation, explainability and interpretability to foster trust for regulatory purposes.

Important Consideration:

- It is crucial to recognise that no single method provides a universal solution for addressing bias and confounding in RWD analysis.
- Researchers must carefully consider their specific data, research question, and potential biases when selecting and applying these techniques.

- Employing multiple methods for sensitivity analysis and transparently documenting the rationale and steps taken is vital for ensuring the credibility and robustness of the generated RWE.

Outcomes Measures from RWD:

- Analysis of RWD allows for the measurement of a variety of outcomes, providing insights into the effectiveness and impact of interventions in real-world settings.[3]
- These outcomes are broadly categorised into primary outcomes and secondary outcomes.
- The primary outcomes reflect the direct impact on patient health, such as clinical outcomes like safety, effectiveness, mortality and patient-reported outcomes.
- The secondary outcomes relate to the broader impact on healthcare systems and resource utilisation, such as resource use, costs and healthcare management.

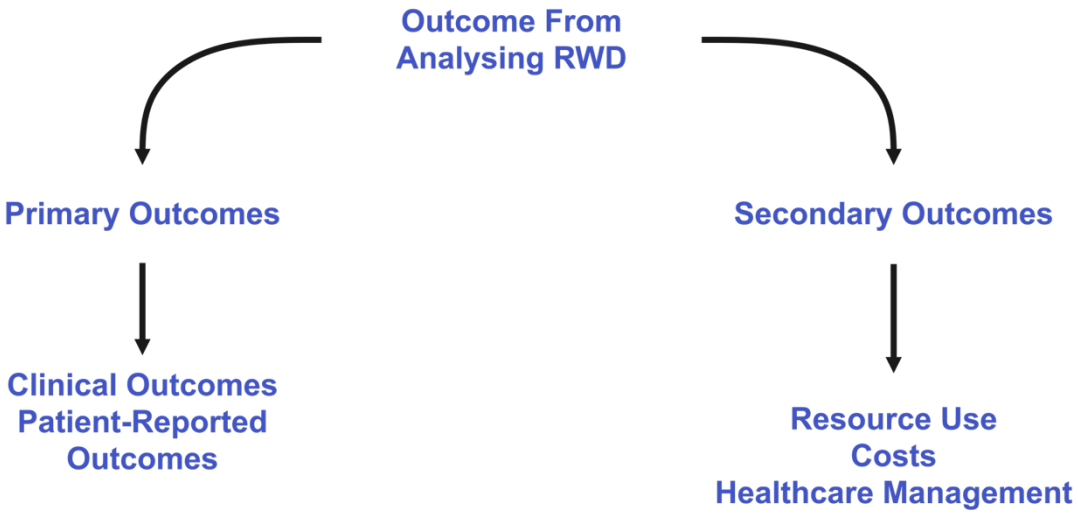

Figure 5.3 Outcome Measures from Analysing RWD

ABBREVIATIONS

Abbreviation	Full Form
AI	Artificial Intelligence
CDMs	Common Data Models
DOSM	Department of Statistics Malaysia
DRG	Diagnosis Related Group
HTA	Health Technology Assessment
IGFMAS	Integrated Government Financial and Management Accounting System
IRBM	Inland Revenue Board of Malaysia
IV	Instrumental Variable
MAHTAS	Malaysian Health Technology Assessment Section
MEA	Managed Entry Agreements
ML	Machine Learning
MOH	Ministry of Health
MPIS	Ministry of Health Pharmacy Information System
MyDRG	Malaysian Diagnosis-Related Group
MyHDW	MyHealth Data Data Warehouse
MyPriMe	My Pharmaceutical Information & Medicine Register
NICE	National Institute for Health and Care Excellence
NIH	National Institute of Health
OHDSI	Observational Health Data Sciences and Informatics
PDPA	Personal Data Protection Act
Peka B40	Protection of Health Scheme for the B40 group
PhIS	Pharmacy Information System
PrCTs	Pragmatic Clinical Trials
PREMs	Patient-Reported Experience Measures
PROs	Patient-Reported Outcomes
PSA	Propensity Score Analysis
QOL	Quality of Life
RCTs	Randomised Controlled Trials
RWD	Real-world Data
RWE	Real-world Evidence

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