ACE position statement on the use of real-world data and evidence to support health technology assessment

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ACE
agency for
care effectiveness

Record of updates

Date	Version	Summary of changes
January 2026	1.0	Publication of initial ACE position statement on the use of real-world data and evidence to support health technology assessment.

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Foreword

Established by the Ministry of Health (MOH), the Agency for Care Effectiveness (ACE) is the national health technology assessment (HTA) and clinical guidance agency in Singapore. It produces evidence-based evaluations of health technologies (e.g. drugs, vaccines and medical technologies) to inform funding decisions by MOH committees, and publishes technology guidance documents for public hospitals and institutions in Singapore to promote the appropriate use of clinically effective and cost-effective treatments. Find out more about ACE at https://www.ace-hta.gov.sg/about-us.

This position statement provides guidance on the use of real-world data (RWD) and real-world evidence (RWE), outlining the circumstances where RWD and RWE may be needed or valuable for evaluating health technologies within ACE's scope.

Information in this statement may be useful for researchers, healthcare professionals, and industry stakeholders involved in collecting RWD, generating RWE, or submitting data or evidence for funding decisions. ACE will continue to review and update this statement to ensure that it remains a useful resource for the Singapore healthcare system.

ACE would like to thank the following experts for their comments during the development of version 1.0 of this guide (appointments listed were current when guide was first published in January 2026):

- Prof Terry Campbell, Emeritus Professor of Medicine, University of New South Wales (UNSW Sydney), Australia
- Prof Jonathan Craig, Vice President & Executive Dean, College of Medicine and Public Health, Flinders University, Australia
- Prof Tracy Merlin, Professor of Health Technology Assessment and Head, School of Public Health, University of Adelaide, Australia
- Dr Sam Roberts, former Chief Executive, National Institute for Health and Care Excellence (NICE), United Kingdom
- Sudha Kutty, Executive Vice-President of Evidence, Products, and Services, Canada's Drug Agency (CDA-AMC), Canada

Abbreviations and acronyms

Term	Definition
ACE	Agency for Care Effectiveness
CTGTP	Cell, Tissue and Gene Therapy Product
HTA	Health technology assessment
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
PREMS	Patient reported experience measures
PROMS	Patient reported outcome measures
RCT	Randomised controlled trial
ROBINS-I	Risk Of Bias In Non-randomized Studies - of Interventions
RWD	Real-world data
RWE	Real-world evidence
TRUST	Trusted Research and Real world-data Utilisation and Sharing Tech

Position statement

1. Background

The use of data to drive healthcare decision-making for drugs, vaccines, cell, tissue, and gene therapy products (CTGTPs) and medical technologies has been growing exponentially, especially with advancements in technology, data collection and analytics, and evolvements in regulatory landscape and policy changes. The fact that health technologies increasingly come with higher costs and/or have limited comparative data is not new, and healthcare systems must make informed decisions on how to integrate them into practice. Results from evidence synthesis of randomised controlled trials (RCTs) remain the gold standard or primary source of evidence for establishing the clinical and cost-effectiveness of health technologies to inform funding decisions due to their rigorous design that minimises confounding and bias. Due to accelerated regulatory approvals based on single-arm trials using surrogate endpoints, health technology assessment (HTA) agencies are increasingly incorporating real-world evidence (RWE) as part of their evaluations, particularly in diseases with a high burden and areas with unmet clinical need, where real-world data (RWD) on the comparator arm helps assess comparative effects (1). RWD also enables the assessment of treatments in the routine practice setting, provide data on real-world outcomes and offer insights into how interventions work across diverse, representative populations. In addition, RWD supports the evaluation of long-term safety and effectiveness, helps track resource utilisation, and informs analyses of healthcare costs and budget impact. In Singapore, RWD and RWE are currently used to provide additional insights into relative effectiveness and safety, or for specific populations, to inform funding decisions (2), to scope the development of the Agency for Care Effectiveness (ACE) clinical guidances (3), and to assess the impact of funding decisions and guidances on clinical practice and patient outcomes (4-6).

2. Definitions of RWD and RWE

We define RWD as data collected outside of controlled trials (e.g. from observational studies, electronic medical records, administrative databases for claims and billing activities, product and disease registries, and patient-generated data including surveys, digital health devices). Different data sources can be linked to improve data quality and fill data gaps, potentially addressing more research questions.

RWE is defined as evidence that is derived from RWD. RWE can inform about the usage and potential benefits or risks of a health technology.

3. Objective

With this position statement, ACE intends to provide guidance on HTA evaluations containing RWD and RWE, and circumstances that increase the necessity or desirability of RWD and RWE and their uses, for the following health technologies within ACE's scope of evaluation:

- Drugs and vaccines
- Highly specialised therapies (such as CTGTPs)
- Medical technologies such as medical devices, medical procedures, imaging tests, digital health technologies

More details on ACE's scope of evaluation, including health technologies outside its remit, can be found in the evaluation or horizon scanning methods and process guide for drugs (7, 8) and medical technologies (9, 10). The statement is targeted at all who are involved in the (i) collection of RWD, (ii) generation of RWE, and/or (iii) submission of data or evidence to inform funding decisions.

4. RWD and RWE applications

RCTs are the preferred source of evidence for funding decisions but these are not without limitations (11). While RWD cannot replace the need for randomised studies, it may generate useful evidence when randomised trials are not feasible or ethical, when the duration of a trial is insufficient to quantify the longer-term treatment effects, when eligibility criteria for the trial are too restrictive and there is uncertainty about the applicability of the findings to the target population, or when the trial evidence does not sufficiently capture the effects of the evolving technology.

The scenarios where RWD can potentially have a role to play in HTA include:

- **Understanding epidemiology, care pathways and resource utilisation**

    a. **Characterising diseases and populations** include aspects such as incidence, prevalence, event rates, natural history of a disease, transition probabilities between disease states and patient demographics
    b. **Treatment characterisation** to understand the current landscape of standard of care, resources utilisation and associated costs (e.g. treatments, diagnostic tests, hospital visits) which can serve as a source of input parameters for economic modelling and budget impact assessments
    c. **Clinical context in HTA decision-making** to understand the potential placement of a new health technology in clinical practice alongside other interventions, which in turn helps to interpret the applicability of the results of the trials to the local clinical setting

- **Assessing how well trial results translate to real world**

    a. **Validating surrogate endpoints**, including but not limited to assessing the biological/scientific association to a clinical outcome, and the connection

between the clinical outcomes and prediction of clinical effectiveness. However, RWD alone rarely suffices for full validation due to confounding and data limitations, and controlled trials are typically needed for primary validation (12).

b. **Measuring the usage and dosing in clinical practice, adherence** to interventions, and **outcomes**
c. **Validating the assumptions applied on longer-term outcomes beyond trial duration.** Trial data may be immature or limited for informing a treatment approach. In this situation, data from observational studies may help to reduce uncertainty around the long-term outcomes, rare safety outcomes or assess safety and effectiveness outcomes in a broader population in line with clinical practice.

- **Providing estimates on effects of a health technology**

a. Where there is a lack of control arm evidence from RCTs due to ethical issues or challenges in patient recruitment, **external control arm** data from other clinical trials or observational studies may be used to estimate relative treatment effects. The selected control arm needs to be comparable with the single-arm trial in several aspects to ensure valid and reliable comparisons. These include matching eligibility criteria, prognostic factors, treatment effect modifiers, outcome measures and definitions, care settings, geographic location, while also reflecting the current standard of care locally (13). The timing of data collection and length of follow-up should align closely with the single-arm trial to reduce temporal biases. Consistency in data collection methods is also important. Furthermore, the use of appropriate statistical methods is needed to adjust for confounding and minimise bias.
b. Where RCTs have excluded certain populations, or they are under-represented, real-world studies may address the gap, and inform the extrapolation of trial results to these target populations
c. Estimating **patient-reported outcomes** not included in the trial e.g. impact on daily function, health-related quality of life or symptoms, patient satisfaction, user acceptance
d. **Understanding available strategic approaches** not considered in RCTs such as the impact of a sequential testing strategy or treatment strategies
e. Estimating the potential impact of **learning curve** on intervention effects, e.g. the intervention effect changes over time as users become more experienced
f. Estimating the potential impact of **iterative changes to characteristics** of the medical technology on its performance over time e.g. device feature, device failure, performance degradation over time, algorithmic drift, interoperability issues, administration technique or protocol

5. Key considerations on the use of RWE in HTA

Several key factors determine the extent of RWE usability in HTA evaluations: data availability, data suitability, provenance and quality, and study design considerations to minimise bias and confounding. It is important to recognise that not all RWE is of the same quality and reliability. On the appropriateness of methods used to generate RWE, real-world studies must adequately address data missingness, inaccuracies, and inherent biases and confounders in

RWD, which arise from the absence of randomisation or choice of study design and can impact the studies' internal validity. RWD collected may not always be representative of the general population and the approach to cohort selection, including the choice of comparator(s), can also affect the observed intervention effects, which in turn impacts the generalisability or external validity of the findings.

Data suitability, crucial for answering the research question, can be assessed through data source provenance[1] and its fitness for purpose[2]. Transparency in reporting is essential for ensuring that ACE can effectively assess whether the data is appropriate and reliable for answering the research question. Pertinent information regarding data suitability can be presented in a structured and concise manner with reference to international standards and best practices.

Data availability and access to RWD are integral to RWE usage. In Singapore, researchers from the healthcare sector and publicly funded research institutions can access RWD managed by research institutions and public sector agencies through Trusted Research and Real world-data Utilisation and Sharing Tech (TRUST). TRUST is a national health-related data governance framework and technical platform that supports health research analytics (14). Ongoing efforts focus on harmonisation of data governance, data interoperability and standardisation, addressing legal considerations for data sharing, data security and addressing privacy concerns, to overcome RWD access barriers. Examples of other sources of data (15) include:

- Administrative: claims, hospital episodes, emergency department visits
- Electronic health records: primary care, specialist care, diagnoses, procedures, medication records, laboratory results, radiology records
- Registry: birth and death, reportable diseases (such as cancer, human immunodeficiency virus, tuberculosis, myocardial infarction, stroke, renal failure), immunisation, medical device, genomics (such as genetic, biomarker status including tumour markers)
- Surveys: patient reported outcome measures (PROMS), patient reported experience measures (PREMS), national population health survey
- Wearables: activity and body function
- Other databases: Health Sciences Authority's adverse event online database

Linking different RWD sources can improve data completeness but also introduces new challenges related to privacy and data harmonisation. Studies leveraging RWD should consider the impact of missing data, inaccurate recording of events, and inconsistent data capture across different sources, which can introduce bias and affect the validity of findings.

When including RWE in HTA reports, the rationale for its use should be detailed and discussed in the context of all available evidence. It should complement RCT data but not replace it. The

[1] Data source provenance is defined by basic attributes such as linkage processes, quality of data collection and measurement, coverage and governance.
[2] Data fitness for purpose is determined by data quality, completeness and accuracy regarding the relevant study population, exposure(s), outcome(s) and the availability of data on key covariates that can address potential confounding.

sources of RWD including the data linkages, sample size and the methods used to collect and analyse RWD should be clearly described. Checklists such as the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) SUITABILITY Checklist for Electronic Health Records data should be used to report data delineation and data fitness for purpose. The report should also provide a summary of the reliability and quality of the data and a risk of bias assessment should be conducted. The use of RWE should adhere to rigorous standards of methodology by applying appropriate methodological choices, addressing uncertainty, maintaining transparency in reporting through established tools e.g. Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) (16), and ensuring generalisability, and relevance to the studied health outcomes. These standards have been comprehensively outlined in the published literature (17, 18).

6. Conclusion

ACE considers RCTs as the preferred source of evidence on relative effectiveness to inform funding decisions. RWE may be considered supplementary evidence when randomised trials are not feasible or ethical, lack sufficient duration to assess long-term effects, have restrictive eligibility criteria limiting generalisability or when the trial evidence does not sufficiently capture the effects of the evolving technology. RWD can also serve as a source of input parameters for economic modelling and budget impact assessments, encompassing treatment patterns, healthcare resource utilisation and costs. This position aligns with other jurisdictions such as Australia (19), Canada (20), France (21), United Kingdom (22), including those in Asia (23) where RWE can be used in similar situations. The extent to which RWE can serve as supportive evidence depends on three key factors: data availability, data suitability, and the robustness of study design and analysis methods used to generate the evidence. This application will likely vary across different evaluations, depending on factors such as the availability and quality of evidence from RCTs, the local applicability of RWE at the time of evaluation, the quality of the RWE proposed, and the type of health technology and size of the intended population.

This position statement serves as a living document, subject to periodic updates as needed. Updates may be triggered by changes in the HTA landscape relating to RWD or RWE changes, such as developments in RWE methodology and emergence of new health technologies.

References

1. IQVIA. HTA Accelerator. HTA reports (single drug assessments) 2021 [Available from: https://www.iqvia.com/solutions/real-world-evidence/health-economics-and-value/hta-accelerator].
2. Agency for Care Effectiveness. ACE technology guidances 2025 [Available from: https://www.ace-hta.gov.sg/healthcare-professionals/ace-technology-guidances#cat~Drug%20Guidances,Medical%20Technology%20Guidances&type~Published&page~1].
3. Agency for Care Effectiveness. ACE clinical guidelines 2025 [Available from: https://www.ace-hta.gov.sg/healthcare-professionals/ace-clinical-guidances-overview/].
4. Agency for Care Effectiveness. Impact stories 2025 [Available from: https://www.ace-hta.gov.sg/about-us/our-impact/impact-stories].
5. Tan SH, Goh LGH, Ong BSK, Ng DSG, Lin L, Ng RCH, et al. Impact of value-driven healthcare strategies for biosimilar adoption: The Singapore story. PharmacoEconomics - Open. 2024;8(5):679-88.
6. Goh LGH, Sun J, Ong BSK, Khoo D, Sum CF, Ng K. Real-world evaluation of sodium-glucose co-transporter-2 inhibitors and dipeptidyl peptidase-4 inhibitors for managing type 2 diabetes mellitus: A retrospective multi-ethnic cohort study. Journal of Diabetes & Metabolic Disorders. 2022;21(1):521-55.
7. Agency for Care Effectiveness. Drug and vaccine evaluation methods and process guide (Version 3.1). 2023.
8. Agency for Care Effectiveness. Procedures and guidelines for company submissions to the Agency for Care Effectiveness for funding consideration (Version 1.6). 2024.
9. Agency for Care Effectiveness. Medical technologies evaluation methods and process guide (Version 3.0). 2024.
10. Agency for Care Effectiveness. Horizon scanning methods and process guide (Version 2.0). 2024.
11. Greenfield S. Making real-world evidence more useful for decision making. Value in Health. 2017;20:1023-4.
12. National Institute for Health and Care Excellence, Canada's Drug Agency (CDA-AMC), Institute for Clinical and Economic Review (ICER), Australian Department of Health and Aged Care, National Health Care Institute (ZIN), Institute for Technology Assessment in Health (IETS), et al. Surrogate endpoints in cost-effectiveness analysis for use in health technology assessment, White paper. 2024.
13. Appiah K, Rizzo M, Sarri G, Hernandez L. Justifying the source of external comparators in single-arm oncology health technology submissions: A review of NICE and PBAC assessments. Journal of Comparative Effectiveness Research. 2024;13(2):e230140.
14. TRUST. Data Access Committee annual report FY2023 [Available from: https://trustplatform.sg/wp-content/uploads/2024/07/TRUST-DAC-Annual-Report-FY2023-Final.pdf].
15. Julian GS, Shau W-Y, Chou H-W, Setia S. Bridging real-world data gaps: Connecting dots across 10 Asian countries. JMIR Medical Informatics. 2024;12:e58548.
16. Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. British Medical Journal. 2016;355:i4919.

17. Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, et al. Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making. Pharmacoepidemiology and Drug Safety. 2017;26(9):1033-9.
18. Wang SV, Schneeweiss S, Berger ML, Brown J, de Vries F, Douglas I, et al. Reporting to improve reproducibility and facilitate validity assessment for healthcare database studies v1.0. Pharmacoepidemiology and Drug Safety. 2017;26(9):1018-32.
19. Pratt N (joint first authors), Vajdic CM (joint first authors), Camacho X, Donnolley N, Pearson S. Optimising the availability and use of real world data and real world evidence to support health technology assessment in Australia. UNSW Sydney, Australia; 2024.
20. Canada H. Health Canada's position on the CADTH guidance for reporting RWE to support decision-making 2023 [Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/announcements/health-canada-position-guidance-reporting-real-world-evidence-supporting-decision-making.html].
21. Vanier A, Fernandez J, Kelley S, Alter L, Semenzato P, Alberti C, et al. Rapid access to innovative medicinal products while ensuring relevant health technology assessment. Position of the French National Authority for Health. BMJ Evidence-Based Medicine. 2024;29(1):1-5.
22. National Institute for Health and Care Excellence. NICE real-world evidence framework. United Kingdom: NICE; 2022.
23. REAL World Data In ASia for HEalth Technology Assessment in Reimbursement (REALISE) working group. Use of real-world data and real-world evidence to support drug reimbursement decision-making in Asia. Abridged version. 2021.