Real-World Evidence Use in Japanese HTA: Insights From Manufacturer Submissions and Public Analyses (2019-2025)

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Objectives

This study evaluates the use of real-world evidence (RWE) in Health Technology Assessments (HTAs) conducted by Japan's Center for Outcomes Research and Economic Evaluation for Health (C2H), comparing utilization between manufacturer submissions and public analyses.

Methods

All HTAs published on the C2H website between April 2019 and August 2025 with a "completed" status were reviewed. HTAs that were suspended, categorized as H5, or in progress were excluded. Publicly available documents were analysed to assess the presence and type of RWE used by manufacturers and/or public analysis groups. The types of data sourced (e.g., healthcare resource utilization [HCRU], costs, epidemiology), databases used, and the degree of RWE adoption in public reviews were documented.

Results

- A total of 39 completed HTAs were identified. Use of RWE was reported in 69% (n=27) of completed HTAs, whereas in the remaining 31% (n=12) RWE use was either not reported or relevant information was unavailable. Among the completed HTAs, 20 used RWE in company submissions, 18 in public analyses, and 11 in both. For 13 assessments, company submission details were not publicly available **(Figure)**
- Oncology (n=5), endocrinology (n=5), and cardiovascular diseases (n=4) were the most common therapeutic areas in which RWE was used overall. In manufacturer submissions, RWE was most frequently applied in endocrinology (n=5), followed by CNS (n=3) and infectious diseases (n=3). In contrast, RWE use in public analyses was reported most often in oncology (n=4), followed by cardiology (n=3) and CNS (n=3) (Table 1)
- Manufacturers primarily used RWE for cost and HCRU inputs (n=15), followed by epidemiology plus cost/HCRU (n=3)
- Public analyses similarly relied on RWE for cost and HCRU (n=11), while only 5 public analysis used RWE for epidemiological data (either alone or combined with costs/HCRU) (Table 1)
- Use of RWE, either by manufacturers or public analyses, is generally restricted to costs, HCRU and epidemiology data. Assessment of lecanemab is the only exception. It is first case of C2H assessment that considered impact on nursing care, and both manufacturer and public analysis used RWE sources to identify relevant data (Table 1)
- Manufacturers mostly used commercial claims databases, with MDV database being most frequently reported (n=6), while public analyses consistently relied on the National Database (NDB) (Table 1)
- More than half (55%) of RWE from manufacturers was reanalysed by public reviewers

Figure 1. Overview of RWE use in completed HTAs in Japan

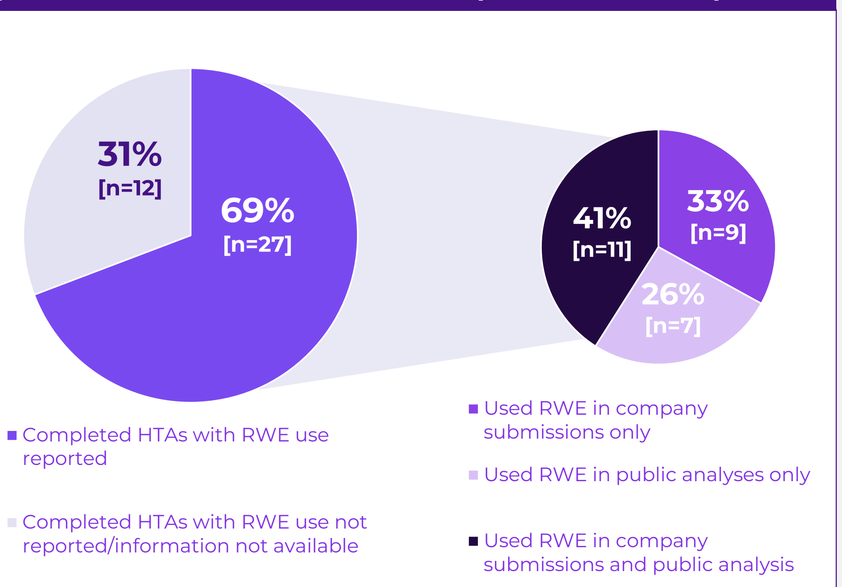

Table 1. Overview of C2H assessments supported by RWE

Product	Year	Disease area	RWE use in manufacturer submission			RWE use in public analysis		
			Y/N	Database used	Domain(s)	Y/N	Database used	Domain(s)
Trelegy (fluticasone, umeclidinium, vilanterol)	2019	Respiratory	Y	NDB	Costs	NR	NR	NR
Ultomiris (ravulizumab)	2019	Rare disease	Y	MDV	Costs	NR	NR	NR
Trintellix (vortioxetine)	2019	CNS	Y	NDB	HCRU	Y	NDB	HCRU
Coralan (ivabradine)	2019	Cardiovascular	NA	NR	NR	Y	NDB	HCRU
Noxafil (posaconazole)	2020	Infectious	Y	NR	NR	Y	NDB	Costs
Rybelsus (semaglutide)	2020	Endocrinology	Y	IQVIA claims database	Costs	Y	NDB	Costs
Cabometyx (cabozantinib)	2020	Oncology	NA	NR	NR	Y	NDB	Epidemiology, Costs, HCRU
Enhertu (trastuzumab deruxtecan)	2020	Oncology	N	NR	NR	Y	NDB	Costs
Emgality (galcanezumab)	2021	CNS	Y	JMDC	Epidemiology, Costs, HCRU	Y	NDB	HCRU
Darzquro (daratumumab vorhyaluronidase alfa)	2021	Oncology	Y	MDV	Costs, HCRU	Y	NDB	Epidemiology, Costs
Micra AV (transcatheter pacing systems)	2021	Cardiovascular	Y	NR	Costs	Y	NDB	Costs
Retevmo (selpercatinib)	2021	Oncology	N	NR	NR	Y	NDB	Epidemiology
Pivlaz (clazosentan sodium)	2022	Cardiovascular	Y	MDV	Costs	NR	NR	NR
Kerendia (finerenone)	2022	Endocrinology	Y	MDV	Costs	N	NR	NR
Lagevrio (molnupiravir)	2022	Infectious	Y	MDV	Epidemiology, Costs, HCRU	N	NR	NR
Sotyktu (deucravacitinib)	2022	Dermatology	Y	Medical Fee Schedule, DPC	Costs	Y	NDB	HCRU
Tezspire (tezepelumab)	2022	Respiratory	Y	NR	Costs	N	NR	NR
Mounjaro (tirzepatide)	2022	Endocrinology	Y	JMDC, Medical Fee Schedule	Costs	N	NR	NR
Xocova (ensitrelvir fumaric acid)	2022	Infectious	Y	JMDC, unspecified domestic claims database, JAMDAS	Epidemiology, Costs	N	NR	NR
Bimzelx (bimekizumab)	2022	Dermatology	NA	NR	NR	Y	NDB	HCRU
Vyvgart (efgartigimod alfa)	2022	Immunology	NA	NR	NR	Y	NDB	Epidemiology
Ondexxya (andexanet alfa)	2022	Cardiovascular	NA	NR	NR	Y	NDB	Epidemiology
Besremi (ropeginterferon alfa-2b)	2023	Oncology	Y	NR	Costs, HCRU	Y	NDB	Costs, HCRU
Litfulo (ritlecitinib tosylate)	2023	Immunology	Y	Unspecified claims database	Costs	Y	NR	NR
Leqvio (inclisiran)	2023	Endocrinology	Y	MDV	Costs	Y	NDB	Costs
Wegovy (semaglutide)	2023	Endocrinology	Y	Unspecified claims and health insurance database, DPC	Costs	N	NR	NR
Leqembi (lecanemab)	2023	CNS	Y	Life study	Long term care	Y	Long term care insurance database	Long term care

Conclusions

- **The majority of completed HTAs in Japan incorporated RWE to some extent**, with comparable frequency across manufacturer and public analyses
- **Manufacturers used a variety of commercial databases** based on their specific needs, while the **public analysis group** consistently—and unsurprisingly—relied solely on the **NDB**, the most accessible resource for its members.
- These divergent data source preferences together with **frequent public reanalysis** suggest the importance of aligning RWE strategies with local expectations.
- **Early integration of NDB-compatible data may strengthen submission credibility** in Japan's HTA process in consequence allowing greater **predictability of public analysis outcomes**

Abbreviations: C2H, Center for outcomes research and economic evaluation for health; CNS, central nervous system; DPC, diagnosis procedure combination; HCRU, healthcare resource utilization; HTA, health technology assessment; JAMDAS, Japan Medical Data Survey database; JMDC, Japan Medical Data Center; MDV, Medical Data Vision; NA, not available; NDB, national database (of health insurance claims and specific health checkups of Japan); NR, not reported; RWE, real-world evidence;

References

1. C2H website https://c2h.niph.go.jp/en/ (Accessed August 2025)

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