

From Regional Principles to Local Implementation: How China’s NHSA and Japan’s C2H Guidelines Build on the Asia Pacific REALISE Guidance for RWE Use in HTA

Wee YR,¹ Yin C,¹ Fujita N,¹ Lim A,¹ Evans JS¹

¹Costello Medical, Singapore



Objective

To review guidance from health technology assessment (HTA) bodies in China and Japan regarding the use of real-world evidence (RWE) for healthcare decision-making.

Background

- The potential of RWE to inform HTA decision-making is increasingly recognised. Several HTA bodies have developed formal guidance to support best practices in the generation, reporting and use of RWE for HTA decision-making, including the United Kingdom¹ and Canada.²
- In Asia-Pacific, the regional REAL world data In aSia for hEalth technology assessment in Reimbursement (REALISE) guideline was published by an expert working group in 2021, providing non-binding guidance intended for local adaptation.³ In 2023, we compared the consistency of REALISE against guidelines issued by regulatory and HTA bodies globally and observed overall agreement.⁴
- This research aimed to assess whether current guidance from HTA bodies in China and Japan align with and build on the regional REALISE guidelines.

Methods

- Guidelines on RWE use by China’s National Healthcare Security Administration (NHSA) and submission guidance from Japan’s Center for Outcomes Research and Economic Evaluation for Health (C2H) were identified through searches of the organisations’ websites in April 2026.
- Each guidance document was reviewed and mapped against the REALISE guidance. Sections from local guidance were categorised as “agree”, “mixed”, “disagree” or “missing” based on coverage and alignment with REALISE.

Results

- China’s NHSA had released six guidelines in 2026 which provide an extensive framework for generating and evaluating HTA-oriented RWE to support reimbursement decision-making in China (Figure 1). Conversely, C2H had not published any standalone RWE guidance, but did include minimal references to RWE within its submission dossier guidance from 2024–2025.
- No guidance disagreed with REALISE; misalignments were largely in terms of coverage. Table 1 maps each country’s guidance coverage against sections of REALISE, illustrating the NHSA’s comprehensiveness vs C2H’s minimal guidance.
- For China, 23% of sections were mapped as “agree”, 41% were “mixed”, and 36% were “missing”. There was strong alignment between NHSA guidelines and REALISE on high-level RWE principles, such as research transparency and methodological rigour.
- Sections mapped as “mixed” largely reflected differences in granularity, with REALISE providing high-level regional guidance while Chinese guidelines offered implementation-specific detail. Similarly, sections mapped as “missing” from REALISE largely contained China-specific implementation details that were out of scope of REALISE (selected examples in Table 2).
- For Japan, RWE was only mentioned in the context of its incorporation within discrete sections of the HTA submission dossier, without any specifics on C2H preferences. Among the limited sections within C2H guidance that discussed RWE concepts, 33% “agreed” with REALISE, while 67% mapped as “mixed”. As illustrated by the quotes in Table 2, C2H guidance focused on providing some broad recommendations on the reporting of RWE, highlighting its limitations, whereas REALISE contained a lengthier discussion of potential usage scenarios including both benefits and limitations of RWE.

Conclusions

While neither NHSA nor C2H had any misalignments with REALISE on overarching principles, NHSA’s comprehensive guidelines build on REALISE by detailing processes, preferences and requirements specific to China’s HTA context.

The detailed guidance provided by China’s NHSA provides clear pathways for the incorporation of RWE in reimbursement decision-making, and signals support for the growing role of high-quality RWE in HTA.

On the contrary, despite Japan’s relatively mature RWE landscape, the lack of RWE-specific guidance from Japan’s C2H suggests a potentially more conservative role for RWE in Japanese HTA.

FIGURE 1

Comprehensive framework outlined by six NHSA RWE guidelines

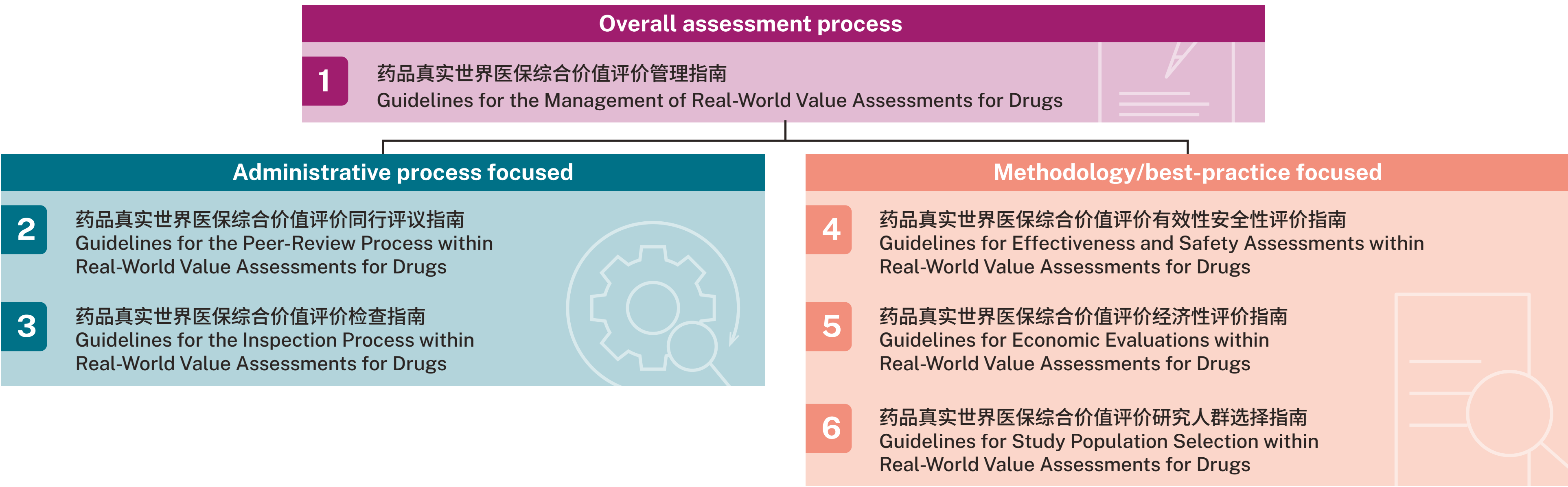


TABLE 1

NHSA and C2H coverage comparison against REALISE

	China (NHSA)	Japan (C2H)
Sections from REALISE*		
RWD and RWE definitions		
Complementing interventional data		
Application to rare diseases		
Surrogate vs final end-points		
Biases/limitations of RWD/RWE		
Data quality considerations		
Recommendations to increase data quality		
Confounding		
Selection bias		
Missing data		
RWD sources		
Disease registries		
Claims databases		
EMRs		
Health surveys		
Wearables and personal tracking devices		
Study designs and good practice guidelines		
Observational studies		
Pragmatic clinical trials		
Single arm trials		
RWD governance and accountability		
Standardisation of variables between sources		
Statistical methods to analyse RWD		
Propensity score analyses		
Covariate adjustment		
Instrumental variables		
Imputation for addressing missing data		
Net benefit regression		
Uses for reimbursement decision-making		
Extrapolating beyond RCTs		
Localising economic models		
Re-evaluating initial reimbursement decisions		
Price negotiations or managed entry schemes		
Integrating RWD in economic evaluations		

*Some sections of REALISE were combined into key topics for this figure. Subsections that contained a mix of “mixed”, “missing” or “agree” tags were mapped as “mixed” in this figure for simplicity. Blue: agree; yellow: mixed; white: missing.

Abbreviations: C2H: Center for Outcomes Research and Economic Evaluation for Health; HTA: health technology assessment; NHSA: National Healthcare Security Administration; RCTs: randomised controlled trials; RWD: real-world data; RWE: real-world evidence.

References: ¹NICE. NICE Real-World Evidence Framework. 2022; ²CDA-AMC. Guidance for Reporting Real-World Evidence. 2023; ³REALISE Working Group. Use of Real-World Data and Real-World Evidence to Support Drug Reimbursement Decision-Making in Asia. 2021; ⁴Wee, YR et al. Keeping it real around the world: Comparing regulatory and HTA RWE guidance. ACPE. 2023. Acknowledgements: The authors thank Niki Lim, Costello Medical, for graphic design assistance.

TABLE 2

Illustration of notable differences in coverage between regional and local guidance for RWE use in HTA

REALISE regional guidance ³	Local HTA guidance
Broad principles: “... the involvement of key stakeholders (e.g., patients, clinicians, clinical administrators, HTA/payers, regulators, and manufacturers) would be meaningful in designing, conducting, and disseminating RWD research... It is important to promote transparent and honest dialogue among stakeholders regarding the use of RWD/RWE, and to have commitment from research funders as well as providers and professional associations at all levels (national and regional) to support the development of infrastructure for collecting and analyzing RWD in the region.”	NHSA describes a structured engagement and scientific review process - Sponsors and initiators should complete an initial consultation with NHSA prior to formal commencement of the RWE study, where authorities would evaluate the proposed study protocol, before the protocol is formally pre-registered on an NHSA-specific platform. NHSA consultation is also required for any protocol amendments 1 - After study report finalisation, a peer-review process will be organised by NHSA to evaluate scientifically rigorous study designs, appropriate study conduct, and robust study conclusions, to be conducted by blinded, independent academic experts 2 - A research inspection process may be initiated if specific scientific concerns or compliance risks are identified during peer-review 3 NHSA describes specific incentive mechanisms for high-quality RWE - If a study is terminated without justification, or if results are not disclosed appropriately, an official record of non-compliance will be logged for the sponsor and investigator 1 - Price-negotiation incentives may be provided for new drugs where high-quality, fit-for-purpose RWE is submitted; conversely, price reassessments may occur if expected evidence is not delivered 1 - Potential funding support from HTA or payer bodies for real-world studies with high public value 1 No coverage in C2H guidance
Dedicated section (“Scenarios to use RWD/RWE: When might be appropriate to consider RWD/RWE for reimbursement decisions?”) discussing suggestions and citing past global use-cases: “Common examples where RWD may be useful include validating the choice of survival curve drawn from studies conducted in other settings, utilizing local data for parameters into economic models, and re-evaluating reimbursement decisions...”	NHSA discusses several types of application scenarios for RWE in effectiveness and safety assessments and within economic evaluations, with recommendations for what studies should focus on and what RWE can inform in each scenario 1 4 5 6 C2H guidance comprises a brief note: “As a general rule, the results of non-RCTs should be used to complement the results of an RCT to evaluate the benefits of the product.”
High-level methodological considerations: “Determine the choice of study design (observational studies, pragmatic clinical trials) with considerations of access and completeness of local RWD sources, and the time available to collect the data to inform the research question; Use a long enough timeframe of RWD collection beyond the pivotal RCT to allow longer-term safety and efficacy outcomes to be captured.”	NHSA details extensive and explicit guidance on how to best align with decision-making requirements and evidence needs Some specific examples include: - Multicentre studies are encouraged; studies with 2–3 sites should include at least one NHSA-approved trusted site, and studies with ≥3 sites should include at least two trusted sites 1 - Mandated use of specific standardised study report template and study registration platform and repository 1 C2H provides minimal guidance, focused on reporting: “More various biases tend to occur in the non-RCTs than in the RCTs. Sufficient explanation of research quality is required (e.g., study design, differences in background factors between groups, statistical analysis, sample sizes, and number of institutions).”

Numbered icons refer to NHSA guidelines 1 to 6 (as detailed in Figure 1).