

Comparisons of economic evaluation guidelines between Japan and 6 other countries (England, France, Germany, Sweden, Canada, and Australia)

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Background and objective

- In Japan, the initial program to introduce HTA was piloted in 2016, starting with economic evaluation. HTA was officially introduced in April 2019. The cost-effectiveness committee at the Central Social Insurance Medical Council (Chuikyō) released the first guideline for economic evaluation in 2016 and updated it in 2019 and 2022
- This study compared Japanese HTA guidelines with current HTA guidelines in 6 countries with more established HTA practices to identify similarities and differences between Japanese and other major HTA guidelines

Methods

- Guidelines from Japan, England, France, Germany, Sweden, Canada, and Australia on methods for conducting HEE were identified. All key HEE elements were compared between the countries to distinguish differences in requirements, especially between Japan and the other markets

Results

- All results are presented in the Table. Differences between Japan and other countries are indicated by a star ★
- Japan is unique in using HEE only to adjust the reimbursed price after initial listing and only for select products. It is most like Germany, where HEE is used only for pricing. The other 5 countries use HEE for both reimbursement and pricing decisions
- For most HEE elements, the HTA bodies are prescriptive, with time horizon as a noticeable exception. The advice is to ensure it is long enough to capture all relevant outcomes, which will depend on the disease in question

Table. Main criteria in pharmacoeconomic guidelines in Japan, England, France, Germany, Sweden, Canada, and Australia

Item ^a	Japan: C2H (1)	England and Wales: NICE (2)	France: HAS-CEESP (3-5)	Germany (IQWiG/G-BA) (6,7)	Sweden: TLV (8-11)	Canada: CADTH (12-14)	Australia: PBAC (15,16)
HEE mandatory for HTA	Mandatory Used to adjust the price after entry to national reimbursed drug list	Mandatory Used to determine entry to national reimbursed drug list ★	Not always mandatory (only in specific cases) Used to assist defining initial price for entry to national reimbursed drug list ★	Not mandatory (only in rare cases) Used to inform price negotiations if standard process has failed ★	Mandatory Used to determine entry to national reimbursed drug list ★	Mandatory Used to determine entry to national reimbursed drug list ★	Mandatory Used to determine entry to national reimbursed drug list ★
Population	Population defined during the scoping phase	Population defined during the scoping phase	Population recommended for reimbursement by CT/CNEDI/MTS ★	Population defined during the scoping phase	Population for which reimbursement is requested ★	Licensed indication (+SA with reimbursement-requested population) ★	Population for which reimbursement is requested ★
Economic comparator	Most commonly used or standard therapy Need to agree with C2H	All clinically relevant comparators defined during the scoping phase ★	All clinically relevant comparators ★	The clinically relevant comparator used in the preceding benefit assessment [+SA with other comparator(s)] ★	Most cost-effective of the clinically relevant comparators ★	All clinically relevant comparators ★	Main comparator (i.e., therapy/therapies most likely to be replaced) ★
Accepted analytical techniques	Base case: CUA, CEA, or CMA Key results measure: ICER (Δ cost/Δ QALY)	Base case: CUA or CCA Key results measures: ○ ICER (Δ cost/Δ QALY) ○ Net health benefits	Base case: CUA + CEA, CEA alone, or CMA (possible in theory, but not in practice) Key results measures: ○ CUA: ICER (Δ cost/Δ QALY) ○ CEA: ICER [cost/lifetime indicators (e.g., life years, all-cause mortality)]	Base case: CUA or CEA Key results measure: ICER [Δ cost/Δ endpoints of the benefit assessment (weighted, if necessary) or Δ cost/Δ QALY]	Base case: CUA, CMA, or CBA (with WTP as outcome measure) Key results measure: ICER (Δ cost/Δ QALY)	Base case: CUA or CMA (only in specific cases); CCA or CBA as supplementary Key results measures: ○ ICER (Δ cost/Δ QALY) and efficiency frontier ○ Net monetary benefits	Base case: CUA, CEA, or CMA; CCA or CBA as supplementary Key results measures: ○ CUA: ICER (Δ cost/Δ QALY) ○ CEA: ICER (cost/outcome as nominated in CEA)
Perspective	Payer (public)	Healthcare system ★	Healthcare system ^b ★	Restricted societal perspective (GKV insured community) ★	Societal ★	Payer (public)	Healthcare system (public or private healthcare provider and patient) ★
Costs to be included	Direct medical costs ▲	Direct medical costs	Direct medical and non-medical costs ▲★	Direct medical and non-medical costs (reimbursable) + patient costs (non-reimbursable) ▲★	Direct and indirect medical and non-medical costs ★	Direct medical and non-medical costs (reimbursable) ▲★	Direct medical costs ▲
Clinical input data	SLR preferred Highest level of available evidence Local data preferred	SLR required Highest level of available evidence	SLR required Highest level of available evidence	No SLR required, only benefit assessment + TLRs Highest level of available evidence	Direct comparative studies or indirect comparisons based on SLRs Highest level of available evidence	SLR required Highest level of available evidence	SLR required Highest level of available evidence
Explicit WTP threshold?	Yes Used to adjust the price (premium) after entry to national reimbursed drug list Standard products: ¥5 million or less per QALY gained Special consideration: ¥7.5 million or less per QALY gained	Yes Formal WTP: ○ Standard: £20,000-£30,000 per QALY gained ○ Highly specialised technologies: £100,000-£300,000 per QALY gained ○ Severe diseases: £30,000-£51,000 per QALY gained	No Cost-effectiveness is assessed based on its position on the frontier, and an estimated ICER or NB is provided CEESP may categorise the ICER as high, very high, or extremely high ★	No G-BA does not have a formal WTP threshold; instead, the ICER is contextualised: ○ Presentation of sensitivity analyses ○ Comparison with similar HEE ★	No TLV does not have formal WTP Informal WTP depends on disease severity: ○ Low: 250,000 kr per QALY gained ○ Medium: 500,000 kr per QALY gained ○ High: 750,000 kr per QALY gained ○ Very high: 1 million kr per QALY gained ★	No CADTH does not have a formal WTP Informal WTP: CA\$50,000 per QALY gained ★	No PBAC does not have an explicit, formal threshold for funding medicines. Generally, PBAC accepts these ICERs: ○ Medicine: AU\$45,000- AU\$75,000 per QALY gained ○ Vaccine: AU\$15,000 per QALY gained ○ Rare disease therapy: AU\$150,000- AU\$200,000 per QALY gained ★
Preferred method to derive utility	Indirect methods: EQ-5D-5L preferred If unavailable, mapping is allowed	Indirect methods: Preferred instrument is EQ-5D-5L, but preferred value set is for EQ-5D-3L If unavailable, mapping is allowed	Indirect methods: EQ-5D-5L (preferred) or EQ-5D-3L If unavailable, mapping is allowed	Direct methods: TTO, SG Indirect methods: ○ EQ-5D VAS or general population utility values are potentially usable ○ Only allowed if validated German tariff is available Mapping is not recommended	Direct methods: TTO, SG, RS Indirect methods: EQ-5D Direct valuation preferred over population (e.g., EQ-5D social tariff)	Indirect methods: EQ-5D, HUI, SF-6D	Indirect methods based on generic classification system (e.g., HUI2 or HUI3, EQ-5D, SF-6D, AQL) Mapping is allowed
Discounting costs and outcomes	Base case: 2% Sensitivity analysis: 0%-4%	Base case: 3.5% Sensitivity analyses: 1.5% ★	Beyond 1 year: 2.5% After 30 years: Discount rate gradually decreases to 1.5% ★	Base case: 3% ★	Base case: 3% Sensitivity analyses: ○ 0%-5% (both) ○ Costs: 3%; outcomes: 0% ★	Base case: 1.5% Sensitivity analyses: 0% and 3% ★	Base case: 5% Sensitivity analyses: 3.5% and 0% ★
Time horizon	Disease dependent	Disease dependent	Lifetime Specific time horizon (e.g., to defined age or over defined period)	Base case: Disease dependent Sensitivity analyses: 5 years	Lifetime Chronic disease: 1-5 years	Disease dependent	Disease dependent
Sensitivity analyses	PSA when possible Structural uncertainty: scenario analyses	PSA and DSA ★	Parameter uncertainty: PSA and DSA Structural uncertainty: Scenario analyses	Univariate and multivariate DSA and PSA Structural uncertainty: Scenario analyses	Required but not prescribed	PSA DSA not recommended Structural uncertainty: Scenario analyses	Univariate and multivariate DSA and PSA
Equity considerations in HEE	None specified	Additional QALY has the same weight regardless of the other characteristics of individuals receiving health benefit, except in specific circumstances ★	None specified	None specified	Caution with productivity losses to void discriminating against people not participating in the labour force ★	Weight all outcomes equally, but report if costs/outcomes differ in subgroups defined by equity-related characteristics and identify groups likely to be disadvantaged ★	None specified
BIA	Optional Time horizon: Not stated	Mandatory, but not for decision-making Time horizon: 5 years	Mandatory only in specific cases ^c Time horizon: 3-5 years ★	Mandatory Time horizon: 3 years ★	Optional Time horizon: not stated	Mandatory Time horizon: 4 years ★	Mandatory Time horizon: 6 years ★

^aBase case unless otherwise stated

^bReference case should be based on collective perspective (patients, healthcare system users, informal caregivers) or, failing that, healthcare system perspective (patients, healthcare system users)

^cBIA is mandatory only for products that are eligible for an economic evaluation and with an estimated revenue of €50 million or more in the second year of marketing; in other cases, it is not mandatory but highly recommended

▲ Countries that allow the incorporation of indirect costs in supplementary analyses

★ Requirements that are different between Japan and other countries

CONCLUSIONS

- Japanese HEE requirements are largely aligned with those in more established HTA markets
- Between all 7 countries, small variations are seen in some technical details (e.g., discount rates) that reflect the national contexts, but there is no greater difference between Japan and the more established HTA bodies than amongst those HTA bodies themselves
- Overall, there is a gap in equity considerations among guidelines. Only the United Kingdom, Sweden, and Canada address equity; they do not provide any detailed insight

Abbreviations: AQL, assessment of quality of life; CADTH, Canadian Agency for Drugs and Technologies in Health; C2H, Center for Outcomes Research and Economic Evaluation for Health; CBA, cost-benefit analysis; CCA, cost-consequence analysis; CEA, cost-effectiveness analysis; CEAC, cost-effectiveness acceptability curve; CEESP, Commission d'Évaluation Économique et de Santé Publique; CMA, cost-minimisation analysis; CNEDI/MTS, Commission Nationale d'Évaluation des Dispositifs Médicaux et Technologies de Santé; CT, Commission de la Transparence; CUA, cost-utility analysis; DSA, deterministic sensitivity analysis; EQ-5D, EuroQol 5 dimensions; EQ-5D-3L, EuroQol 5 dimensions 3 levels; EQ-5D-5L, EuroQol 5 dimensions 5 levels; G-BA, Gemeinsamer Bundesausschuss; GKV, Gesetzliche Krankenversicherung; HAS, Haute Autorité de Santé; HTA, health technology assessment; HEE, health economic evaluation; HUI, Health Utilities Index; ICER, incremental cost-effectiveness ratio; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; NB, net benefit; NICE, National Institute for Health and Care Excellence; PBAC, Pharmaceutical Benefits Advisory Committee; QALY, quality-adjusted life year; QWB, quality of well-being; PRO, patient-reported outcome; PSA, probabilistic sensitivity analysis; RS, rating scale; SA, scenario analysis; SF-6D, Short-Form 6 Dimensions; SG, standard gamble; SLR, systematic literature review; TLR, targeted literature review; TLV, Tandvärds- och läkemedelsformansverket; TTO, time trade-off; VAS, visual analogue scale; WTP, willingness to pay

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