Are There Intersections in Evidence Requirements for Health Technology Assessment Agencies across North America, Europe and the Asia-Pacific?

HTA17

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SUMMARY

OBJECTIVES

- The HTA process has been widely adopted across the world to evaluate the clinical and economic value of interventions, inform pricing and reimbursement decisions, and ensure patient access to evidence-based care.
- This study aimed to present a broad overview of the clinical and economic evidence requirements of HTA agencies across the globe.

METHODS

- The websites of 10 global HTA agencies including NICE (**England and Wales**), NCPE (**Ireland**), JCA (**Europe**), JNHB (**Denmark, Finland, Iceland, Norway,** and **Sweden**), CDA-AMC (**Canada**), ICER (**United States of America**), MSAC (**Australia**), ACE (**Singapore**), C2H (**Japan**) and HITAP (**Thailand**), were searched for published documents and recommendations concerning HTA submissions. Details were extracted and summarised.

RECOMMENDATIONS

- Of the 10 HTA agencies investigated, only **NICE and CDA-AMC** have released position statements concerning the use of **artificial intelligence methods in evidence generation.** NICE stating that organisations should engage beforehand to discuss their plans and comply with the UK AI Government framework and CDA outlining 2 key conditions for AI use (**Table 1**).
- All nine countries require a systematic method of evidence generation as part of the HTA submission, which always included a review of clinical data, with or without a review of economic evaluations, cost and healthcare resource use data, health-related quality of life data and/or health state utility values data.
- The clinical SLR requirements of most countries largely align with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) reporting guidelines. Following pre-existing best practice SLR guidance i.e., Cochrane recommendations, will allow for a transparent, reproducible SLR that is accepted across global HTA organisations.
- In terms of economic modelling requirements, Canada, the UK, Singapore and Japan adopt similar methodologies with variations in choice of perspective, discounting rate, and willingness-to-pay thresholds.

BACKGROUND & AIMS

- Systematic literature reviews (SLRs) of published and unpublished literature play a vital role in the health technology assessment (HTA) process by establishing a robust evidence base for decision-making.
- This study aimed to provide a comprehensive overview of the commonalities and variations in clinical evidence and health economic (HE) modelling requirements across HTA bodies in North American, European, and Asia-Pacific countries.

METHODS

- 10 HTA agency websites – NICE (England and Wales), NCPE (Ireland), JCA (Europe), JNHB (Denmark, Finland, Iceland, Norway, and Sweden), CDA (Canada), ICER (United States of America), MSAC (Australia), ACE (Singapore), C2H (Japan) and HITAP (Thailand) – were comprehensively searched to identify specific guidance for SLRs and HE modelling in HTA.[1-10]

RESULTS

- All assessed HTA agencies agreed on the need to identify, synthesise, and document clinical evidence in a systematic, reproducible way (**Table 2**).
- On HE modelling, most agencies preferred cost-utility analyses, generic utility instruments, uniform discounting, outcomes expressed in quality-adjusted life years, and exploration of uncertainty through sensitivity analyses (**Table 3**).

Table 1. Evidence requirements for HTA agencies across the globe.

Submission requirement	England and Wales	Ireland	N.Europe	Europe	Canada	USA	Australia	Singapore	Japan	Thailand
	NICE	**NCPE**	**JNHB**	**JCA**	**CDA-AMC**	**ICER**	**MSAC**	**ACE**	**C2H**	**HITAP**
Position statement on the use of AI/ML in SLRs	✓	✘	✘	✘	✓*	✘	✘	✘	✘	✘
SLR of clinical data for the technology	✓	✓	✓	✓	✓	✓	✓*	✓*	✓*	✓
SLR of economic models for technology	✓	✘	✘	✘	✘	✓	✘	✓**	✘**	✘
SLR of cost and resource use data	✓	✓*	✘	✘	✘	✘	✘	✘	✘	✘
SLR of HRQoL/ utility data	✓	✓**	✘	✘	✘	✓	✘	✘	✓***	✘

Table 2. Comparing clinical literature review requirements of HTA agencies across Europe, North America, and the Asia-Pacific.

Type of SLR methodology	Europe	Canada	USA	Australia	Singapore	Japan
	JCA	**CDA-AMC**	**ICER**	**MSAC**	**ACE**	**C2H**
PICOS framework	✓	✓	✓	✓	✓	✓
Permitted clinical trials	**All relevant data**	**Pivotal studies, phase 3/4 RCTs, other study designs on case-by-case basis**	**All relevant data**	**RCTs most valid. If unavailable, other 'lower level' study designs are acceptable**	**RCTs most valid. If unavailable, non-randomised studies may supplement**	**RCTs, unpublished clinical trials. If unavailable, comparative non-RCT and indirect comparison through SLR**
Literature search strategy	**Key biomedical databases, clinical trial registries, subject-specific or individual pharmaceutical company study registries. Systematic, transparently reported search with justified limits. 3-month cut-off date**	**Key biomedical databases and grey literature**	**Key biomedical databases, discipline-specific databases. Well-constructed search strategies**	**Key biomedical databases, HTA agency websites, unpublished studies, citation searching. Broad search strategies, cautious use of search filters**	**Key biomedical databases and INAHTA. Reproducible search strategy**	**Description of databases and search strategy formula required**
Study selection	**Double review**	**Double review**	**Double review by independent reviewers**	**Double review**	**Transparent criteria and procedures**	**Double review**
Reason for inclusion/ exclusion reporting	✓	✓	✓	✓	✓	✓
PRISMA flow diagram	✓	✓	✓	✓	✓	✓
Details of included studies (per PICO)	✓	✓	✓	✓	✓	✓
Methodological quality assessment	✓	✓	✓	✓	✓	✘

Table 3. Comparing HTA agency economic modelling requirements across North America, Europe and the Asia-Pacific.

Type of SLR methodology	CDA-AMC	NICE	ACE	C2H
Type of economic evaluation	**CEA/CUA**	**CEA/CUA/CCA***	**CUA/CEA/CMA***	**CEA/CMA***
Economic modelling required	**Yes ICER approach considered**	**Yes ICER approach considered**	**Yes ICER approach considered**	**Only if SLR shows intervention not inferior to comparator; ICER approach considered**
Willingness-to-pay threshold	**No fixed/explicit WTP. Conclusions and price reductions no longer focus on a single WTP**	**£20,000-£30,000 per QALY**	**No fixed/explicit WTP for healthcare interventions**	**Fixed WTP threshold used - ¥5 million per QALY (range: ¥5 million to ¥10 million per QALY). If ICER for a product > ¥5 million per QALY, price is not adjusted**
Perspective	**Public payer**	**NHS and PSS**	**Singapore healthcare system (government, insurance provider and patient healthcare costs)**	**Standard: Public healthcare payer Public long-term care costs: public healthcare and long-term care payer**
Discounting	**Costs: 5% Outcomes: 5%**	**Costs: 3.5% Outcomes: 3.5%**	**Costs: 3% Outcomes: 3%**	**Outcomes: 2% per year Costs: 2% per year**
Measuring/ valuing outcomes	**Preference-based measures preferred QALYs**	**EQ-5D QALYs**	**EQ-5D, QALYs, LYG Other accepted: SF-36, HUI 3, AQoL**	**Preference-based measures preferred i.e., Japanese version of EQ-5D-5L, QALYs, mapping of other appropriate HRQoL using MAPS checklist**
Uncertainty	**DSA and PSA**	**DSA (scenario analysis) and PSA**	**One-way DSA & Multivariate or PSA**	**PSA**

Table 1 notes:

- *NCPE*

**costs must be identified using a systematic method*

*** explicitly specifies SLR is not limited to utility data only*

- *CDA-AMC: position statement on the use of AI in HTA includes 2 key sections – the 1st outlining the potential uses of AI for HTA-related purposes for all users, and the 2nd outlining the responsibilities of those who use AI methods in the generation and/or reporting of evidence.*
- *ICER: reports include a systematic review of the published clinical and economic literature on a given intervention, including existing high-quality systematic reviews or health technology assessments*
- *MSAC:*

**systematic search required in full HTA only*

- *ACE:*

**existing clinical studies, ongoing studies should be mentioned, implicit requirement for an SLR of clinical data*

***comprehensive search of published economic studies, cost-effectiveness of intervention relative to its comparator(s)*

- *C2H:*

**acceptable to use existing reliable SLR with most recent literature directly or in combination with a new literature search*

***cost-effectiveness analysis of a selected product published in an academic journal or reports by a HTA agency*

****SLR of 'QoL data', utility data not explicitly stated*

Table 3 notes:

- *NICE*

**Cost-utility analyses routinely used with an NHS PSS perspective. When possible, NICE programmes use cost-effectiveness analysis to compare between programmes. If outcomes cannot be expressed in utilities, a cost-consequences analysis may be considered.*

- *ACE:*

**Cost-minimisation analysis considered for expedited and full evaluations when relevant*

- *C2H:*

**Cost-minimisation analysis considered if an intervention does not demonstrate additional benefits*

References

1. *NICE. NICE health technology evaluations: the manual. 2022;* ***2.*** *NCPE requirements for conducting and reporting clinical evidence synthesis analyses.* ***3.*** *JNHB submission dossier template.* ***4.*** *EU JCA. Template for the dossier of the Joint Clinical Assessment of a medicinal product.* ***5.*** *CDA-AMC. Guidelines for the Economic Evaluation of Health Technologies: Canada (4th Edition). 2017.* ***6.*** *ICER. A Guide to ICER's Methods for Health Technology Assessment.* ***7.*** *MSAC. Guidelines for preparing assessments for MSAC.* ***8.*** *C2H. Guideline for Preparing Cost-Effectiveness Evaluation to the Central Social Insurance Medical Council.* ***9.*** *HITAP. Health Technology Assessment Process Guidelines.* ***10.*** *ACE. Medical Technologies Evaluation Methods and Process Guide.*