Comparative assessment of systematic literature review requirements for health technology assessment, globally

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BACKGROUND

- An integral part of a health technology assessment (HTA) is a systematic literature review (SLR), an unbiased, high-quality synthesis of available evidence.
- For many HTA agencies, guidance on data sources, methodology, required outcomes, and reporting of the SLR varies considerably

OBJECTIVE

- The objective of this study was to conduct a comparative assessment of the clinical and economic SLR methodological requirements of HTA agencies in different countries around the world.

METHODS

- We searched eight HTA agency websites (www.pbs.gov.au [Australia], www.cadth.ca, [Canada], www.nice.org.uk [England], www.has-sante.fr [France], www.g-ba.de [Germany], www.zorginstituutnederland.nl [Netherlands], www.ace-hta.gov.sg [Singapore], www.tlv.se [Sweden]) to identify guidance on the use of SLRs in HTA.
- Relevant information was extracted and compared.

RESULTS

- All eight countries require an SLR of clinical data for the technology and its comparators.
- A quality assessment of included studies and critical appraisal of randomised and non-randomised clinical trials is also requested. Only three countries (Australia, England, and France) requested an SLR of economic models for the technology, with the latter two also requiring a critical appraisal of the models.
- SLRs of utility, resource use, and cost data were less frequently mandated, with only NICE in England suggesting the inclusion of an SLR of utility data (**Table 1**).
- The use of a valid, published tool for quality assessment (QA) of included studies is required by six countries. Most commonly specified QA tools for RCTs were Cochrane/ RoB2 (Australia & Singapore), and for non-RCTs the ROBINS-1 tool (Australia, Germany & Singapore) (**Table 2**).
- Five countries state a clear preference for randomised controlled trials (RCTS) in the search strategy for SLRs. The majority of countries suggest which literature databases to search, most commonly Medline, Embase and the Cochrane library.
  A requirement for transparency in relation to study selection is evident, with seven countries mandating the reporting of details of included and excluded literature (**Table 3**).

Table 1. SLR requirements for HTA submission

	Country	Australia	Canada	England	France	Germany	Netherlands	Singapore	Sweden
		PBAC	CADTH[1–3]	NICE[4]	HAS[5]	IQWIG/G-BA[6]	ZiN[7]	ACE[8]	TLV[9]
Focus of SLR	Clinical data for technology and its comparators	✓	✓	✓	✓	✓	✓	✓	✓
	Economic models for technology	✓	✗	✓	✓	✗	✗	✗	✗
	Resource use and cost data	✗	✓	✓	✗	✗	✗	✓	✗
	Utility data	✗	✗	✓	✓*	✗	✗	✓	✗
Quality assessment and critical appraisal	Quality assessment	✓	✓	✓	✓	✓	✓	✓	✓
	Critical appraisal of RCTs and non-RCTs	✓	✓	✓	✓	✓	✓	✓	✓
	Critical appraisal of economic models	✗	✗	✓	✓	✗	✗	✗	✗

*if not derived from an ad-hoc study specifically designed for the collection of the required quality of life data

Table 2. Quality assessment requirements

	Country	Australia	Canada	England	France	Germany	Netherlands	Singapore	Sweden
		PBAC	CADTH[1–3]	NICE[4]	HAS[5]	IQWIG/G-BA[6]	ZiN[7]	ACE[8]	TLV[9]
Recommended quality assessment method	**RCT**	Cochrane RoB 2	NR	Validated tools specific to the study design and use case	Not specified, but needs to be mentioned	Defined by the basic principles of good clinical practice	GRADE	Cochrane RoB 2	NR
	Non-RCT	ROBINS-1†	NR	As for RCT	As for RCT	ROBINS-1	GRADE, Newcastle Ottawa Scale or Down and Black instrument	Use of validated tool required, examples: ROBINS-I, RoBANS	NR

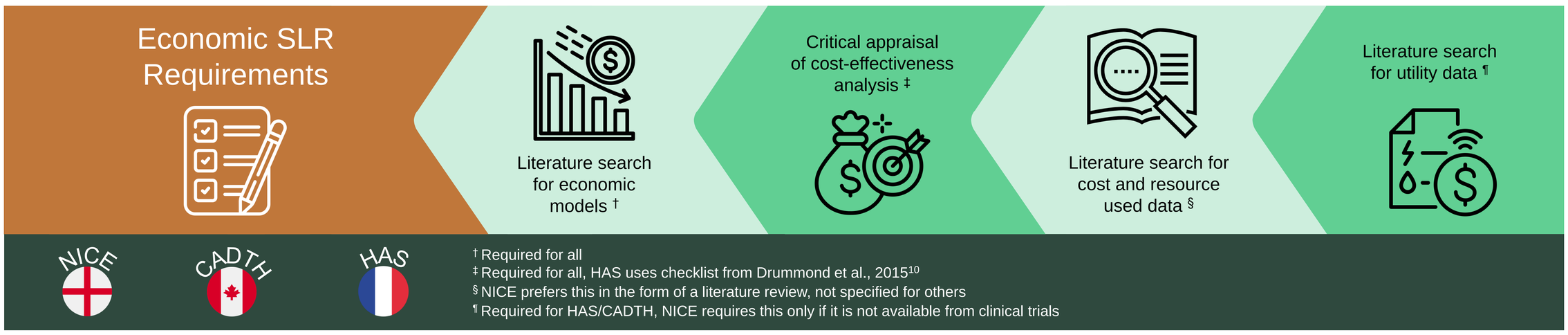
†Advise the use the domains identified in the ROBINS-I tool to organise a discussion of the risk of bias.
NR, Not reported

Table 3. Clinical SLR requirements

	Country	Australia	Canada	England	France	Germany	Netherlands	Singapore	Sweden
		PBAC	CADTH[1–3]	NICE[4]	HAS[5]	IQWIG/G-BA[6]	ZiN[7]	ACE[8]	TLV[9]
Search strategy	Permitted trial types	RCT if available, if not non-randomised	Pivotal studies plus phase 3/4 RCTs – other study designs on case-by-case basis	RCTs preferred, non-randomised may complement where there is a gap in evidence	RCTs preferred, non-randomised if appropriate. Prefer French studies	All relevant studies. English or German language	All relevant publications. RCTs strongly recommended	RCTs most valid. If not available, data from indirect comparisons of RCTs should be considered. When relevant, good quality non-randomised studies can be provided as supplementary evidence	All relevant data
Sources	Databases specified	Medline, Embase, and Cochrane, as a minimum	Cochrane Library, PubMed, NHS CRD Optional: Embase, BIOSIS Previews, CINAHL, PsycINFO	Medline, Embase, Medline (R) In-Process, and Cochrane Library	None specified	Medline, Embase	None specified	Medline (via PubMed), Embase, International HTA database, Cochrane Library	None specified
	Other specified sources	Trial registries, reference lists, marketing approval dossiers, company databases	Trial registries, websites of INAHTA agencies, manufacturers' websites, internet search tools, consultation with experts and agencies	Unpublished data, reference searching, citation searching, inclusion list of systematic reviews, websites	Relevant websites (government agencies, learned societies, conferences), legislative and regulatory texts	Trial registries, manufacturer data, Cochrane library, HTA agency websites, PROSPERO, Dynamed, UpToDate, Pubmed	None	Trial registries, reference lists of relevant articles, grey literature, CSRs, studies pending publication	None
Selection of studies	PICOS	✗	✓	✗	✗	✓	✓	✓	✓
	PRISMA flow diagram	✓	✓	✗	✓	✓	✗	✓	✓
	Report reasons for inclusion and exclusion	✓	✓	✓	✓	✓	✓	✓	✗
	Details of included studies	✓**	✓***	✓	✓	✗	✓	✓	✓

** including how they support the clinical claim; *** including design, population, drugs, study duration, outcomes, publication status. CSR, clinical study report, NR, not reported

Figure 1. Economic SLR requirements



DISCUSSION AND CONCLUSION

- While all eight countries require an SLR as part of the HTA submission, a limited consensus was found in terms of SLR requirements.
- The specific requirements for conducting SLRs in HTAs vary globally due to differences in regulatory frameworks, healthcare systems, and decision-making processes.
- The most stringent requirements were found in England and France.
- Differences between HTA agency guidance is a consideration when carrying out an SLR for use in HTA submissions in global markets.
- Efficiencies in conducting SLRs that can fulfil the requirements for multiple HTA bodies can be made with strategic planning.

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